Johnson, N.
380857

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L3   (        66) SEA FILE=CA L2 AND (?TUMOR? OR ?TUMOUR? OR ?CANCER? OR ?C
                  ARCIN? OR ?NEOPLAS?)
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                  OCYT? OR PBL#)
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                  ARCIN? OR ?NEOPLAS?)
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                  OUND?)


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L6   ANSWER 1 OF 40  CA  COPYRIGHT 1996 ACS            DUPLICATE 1
AN   123:196605  CA
TI   Immuno-stimulatory monoclonal antibodies
SO   PCT Int. Appl., 52 pp.
     CODEN: PIXXD2
IN   Hardy, Britta; Novogrodsky, Avraham
AI   WO 95-US1137  950130
PI   WO 9520605 A1  950803
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PY 1995
AB A monoclonal **antibody** having immuno-stimulatory effects, **binds** specifically to **B lymphoblastoid** cells and induces **proliferation** and **activation** of **peripheral blood lymphocytes**, and when injected into **tumor**-bearing animals elicits an anti-**tumor** effect. In example, monoclonal anti-**B lymphoblastoid** cell **antibodies** were characterized, purified, and used to induce cytotoxicity of peripheral blood mononuclear cells, to stimulate synergistic cytotoxicity with interleukin 2, and to provide immunotherapy effect against **tumor** or lung metastasis.

L6 ANSWER 2 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 2
AN 123:81616 CA
TI Animal model of the human immune system
SO Can. Pat. Appl., 81 pp.
CODEN: CPXXEB
IN Gallinger, Steven; Hozumi, Nobumichi; Roder, John C.; Sandhu, Jasbir S.; Shpitz, Baruch
AI CA 93-2103693 930806
PI CA 2103693 AA 950207
PY 1995
AB The present invention relates to a non-human chimeric mammal having characteristics of a functional human immune system and having functional human lymphocytes reconstituted in the mammal's lymphopoietic tissue, particularly the spleen. The invention also relates to a method of prepg. a non-human chimeric mammal, having characteristics of a functional human immune system, by engraftment of human peripheral blood leukocytes into an immunocompromised mammal. Use of the chimeric mammal as a model of the human immune system is described. In example, engraftment of radiation and anti-ASGM1 **antibody**-treated SCID mice with human peripheral blood leukocytes (**PBL**), functional anal. of the human lymphocyte populations and primary immune response in the Human **PBL**-SCID mice were described.

L6 ANSWER 3 OF 40 CAPLUS COPYRIGHT 1996 ACS
AN 1995:794180 CAPLUS
TI Perinuclear anti-neutrophil cytoplasmic **antibodies** are spontaneously produced by mucosal **B cells** of ulcerative colitis patients
SO J. Immunol. (1995), 155(6), 3262-7
CODEN: JOIMA3; ISSN: 0022-1767
AU Targan, Stephan R.; Landers, Carol J.; Cobb, Linda; MacDermott, Richard P.; Vidrich, Alda
PY 1995
AB Approx. 60% of sera from ulcerative colitis (UC) patients contains lgs reactive with neutrophil components, raising the question of the origin of these anti-neutrophil cytoplasmic Abs (ANCA). Our assertino that ANCA is a marker for a mucosal disease-related immune response predicts the existence of ANCA producing **B cell** clones in the lamina propria lymphocyte (LPL) fractin

of UC patients. This hypothesis was tested by examg. 12-day culture supernatants of LPL ANCA expression. LPL were isoalted from surgically removed mucosa from patients with UC, Crohn's disease (CD), and diverticulitis. Normal mucosa was obtained from accident victims or normal margins of colon **cancer** resections. Supernatants were assayed by a fixed neutrophil ELISA> The ANCA staining pattern of supernatants expressing ANCA, as detd. by ELISA, was assessed by indirect immunofluorescent staining of alc.-fixed neutrophils. ANCA was found in 70% of culture supernatants from UC LPL fractions. In contrast, only approximatley 11% of supernatants from CD and diverticulitis/normal (noninflammatory bowel disease (IBD)) LPL displayed ANCA **binding**. A perinuclear (pANCA) staining pattern was obtained with 70% of ANCA-expressing UC LPL supernatants, whereas ANCA-expressing CD and non-IBD LPL supernatants displayed a cytoplasmic reaction. **PBL** and mesenteric lymph node lymphocytes lacked spontaneous pANCA prodn., and pANCA prodn. from **PBL** was not inducible. These findings indicate the existence of pANCA-producing **B cell** clones in mucosal lesions of UC patients and support our hypothesis that pANCA prodn. is a consequence of a mucosal immune response specific to UC.

L6 ANSWER 4 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 3
AN 122:262012 CA
TI Expression of HOXC4 homeoprotein in the nucleus of **activated** human lymphocytes
SO Blood (1995), 85(8), 2084-90
CODEN: BLOOAW; ISSN: 0006-4971
AU Meazza, Rafaella; Faiella, Antonio; Corsetti, Maria Teresa; Airoldi, Irma; Ferrini, Silvano; Boncinelli, Edoardo; Corte, Giorgio
PY 1995
AB We have analyzed the expression of homeoproteins of the HOX family in resting and **activated** lymphoid cells and in **neoplastic** lymphoid cell lines by the use of monoclonal **antibodies** (MoAbs) already shown to react with the homeoproteins HOXA10, HOXC6, and HOXD4, resp. Anti-HOXA10 and C6 MoAbs DIDi not show any reactivity with the lymphoid cells tested, whereas anti-HOXD4 MoAb stained few resting **peripheral blood lymphocytes** (**PBLs**) and most phytohemagglutinin (PHA)-stimulated **PBLs** as early as 6 h after stimulation. The pattern of staining of PHA-**activated PBLs** in reminiscent of the stages of nucleolar fragmentation in different phases of the cell cycle. The MoAb reacted also with **activated** or Epstein-Barr virus-transformed **B cells**, with clonal or polyclonal T and natural killer (NK) cells, with leukemic T-cell lines, and with a Burkitt's lymphomas cell line. RNAse protection expts., performed with probes specific for HOXD4 or for the highly homologous HOXA4, HOX4, and HOXC4, belonging to the same paralogy group, indicated that only HOXC4 mRNA is present in resting or **activated PBLs**. Northern blot anal. on polyA+ RNA from **activated PBLs** or Raji cells showed the presence of two differen.tau. HOXC4 transcripts of 2.8 and 1.9 kb. Gel retardation and

Southwestern blot assays showed the presence of 32-kD homeoprotein with DNA-.beta.inding properties typical of a HOX4 homeoprotein in nucleolar exts. of PHA-**activated**, but not of resting, lymphocytes. Taken together, these data indicate that the HOXC4 homeoprotein is expressed in **activated** and/or **proliferating** lymphocytes of the T-, B-, or NK-cell lineage, whereas it is weakly expressed in a minority of resting cells. The early expression and the nucleolar localization suggest an involvement of HOXC4 in the regulation of genes controlling lymphocyte **activation** and/or **proliferation.**

L6 ANSWER 5 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 4
AN 123:225834 CA
TI **Activation** of human lymphocytes by a monoclonal **antibody** to **B lymphoblastoid** cells; molecular mass and distribution of **binding** protein
SO Cancer Immunol. Immunother. (1995), 40(6), 376-82
CODEN: CIIMDN; ISSN: 0340-7004
AU Hardy, Britta; Galli, Michal; Rivlin, Eyal; Goren, Liz; Novogrodsky, Abraham
PY 1995
AB A novel monoclonal **antibody** (BAT) to the **B-lymphoblastoid** cell line **activates** murine lymphocytes and exhibits a striking **antitumor** activity in mice. In order to evaluate the potential use of this **antibody** against human **cancer**, we have investigated its immuno-stimulatory properties on human **peripheral blood lymphocytes** (**PBL**). Our findings demonstrate that BAT mAb induces **proliferation** and cytotoxicity in human **PBL** against natural-killer-cell-sensitive and natural-killer-cell-resistant **tumor** cell lines. Interleukin-2 at a low concn. synergizes with BAT mAb in eliciting these effects. BAT mAb **binds** to human peripheral T cells as revealed by a double-labeling technique using anti-CD3 and BAT mAb. The mol. mass of the antigen recognized by BAT mAb was 48-50 kDa under reducing and non-reducing conditions. This study provides a basis for future expts. to evaluate the use of BAT mAb in the immunotherapy of **cancer.**

L6 ANSWER 6 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 5
AN 120:215126 CA
TI High level functional engraftment of severe combined immunodeficient mice with human **peripheral blood lymphocytes** following pretreatment with radiation and anti-asialo GM1
SO J. Immunol. Methods (1994), 169(1), 1-15
CODEN: JIMMBG; ISSN: 0022-1759
AU Shpitz, Baruch; Chambers, Cynthia A.; Singhal, A. Brij; Hozumi, Nobu; Fernandes, Bernard J.; Roifman, Chaim M.; Weiner, Louis M.; Roder, John C.; Gallinger, Steven
PY 1994
AB The severe combined immunodeficient (SCID) mouse engrafted with

human **peripheral blood lymphocytes** (**PBLs**) is a potentially useful model for the study of **cancer** immunotherapy. For this application, rapid, consistent, and high level engraftment of SCID mice with functional human cytotoxic effector cells is necessary. To date, short term human lymphoid cell engraftment in SCID mice has generally been low and variable. Further, most of the human cells detected within the first 30 days are found in the peritoneal cavity. The purpose of the present study was to improve short term reconstitution of human **PBLs** in the SCID mouse. When untreated SCID mice were injected with human **PBLs**, the mean level of CD3+ cells in the spleens was <5% on days 6-32 after injection, as detd. by flow cytometry (FCM). Depletion of SCID mouse natural killer (NK) cells with anti-asialo GM1 only marginally improved short term reconstitution with human CD3+ cells. Preirradn. of SCID mice with 3 Gy improved reconstitution to over 16% CD3+ cells on days 12-14 following engraftment. However, the combination of pretreatment with anti-asialo GM1 plus radiation, significantly increased the mean percentage of human CD3+ cells in the spleen to 40% within 2 wk following injection of **PBLs**. Human T cells pos. for CD4, CD8, TcR.alpha..beta., and TcR.gamma..delta., and human NK and **B cells** were detected in the spleens of irradiated plus anti-asialo GM1 pretreated SCID mice. The presence of human lymphoid cells was confirmed by immunohistol. staining. The human immune cells in these mice were shown to be functional by the in vivo demonstration of an appropriate secondary immune response to the injection of tetanus toxoid and by an in vivo **proliferative** response to phytohemagglutinin. Human NK cells could be found in the spleens and peripheral blood of irradiated plus anti-asialo GM1 pretreated mice. These cells were also shown to be competent by their ability to lyse the human NK sensitive **tumor** targets K562 and MOLT-4 in 51Cr release assays. Thus, pretreatment of SCID mice with radiation plus anti-asialo GM1 significantly improves short term human **PBL** engraftment and provides a potentially useful model for the study of **cancer** immunotherapy.

L6 ANSWER 7 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 6
AN 120:75029 CA
TI A novel 120-kDa antigen shared by immature human thymocytes and long-term-**activated** T cells
SO Eur. J. Immunol. (1994), 24(1), 1-7
CODEN: EJIMAF; ISSN: 0014-2980
AU Fabbi, Marina; Tiso, Micaela; Gangemi, Rosaria M. R.; Favre, Anna; Demartini, Paolo; Bargellesi-Severi, Antonio
PY 1994
AB In this study the authors report the characterization of monoclonal **antibody** (mAb) 8B4/20, raised against immature human thymocytes, that identifies a novel leukocyte antigen. The mol. characterization of the antigen by immunopptn. and immunoblotting yields, under nonreducing conditions, a specific band of 120 kDa which, under reducing conditions, displays a slightly lower mol. mass (110 kDa). MAb 8B4/20 detects a mol. found on the majority of

thymocytes with an inverted gradient of expression when compared to CD3. It appears at high d. on the CD3-/low thymocytes, at reduced d. on the CD3med and double-pos. thymocytes, and is absent on CD3hi and single-pos. thymocytes and on peripheral blood T cells. Immunohistochem. on frozen sections demonstrates cortical staining of the thymic lobules. Flow cytometric anal. of the different subsets of peripheral blood mononuclear cells shows that mAb 8B4/20 detects an antigen expressed only on CD56+/CD16+ natural killer cells and on a fraction of CD14+ monocytes. T cells, **B cells**, erythrocytes, granulocytes, and platelets are consistently neg. The expression of the mol. on **tumor** cell lines does not show lineage restriction. Anal. of phytohemagglutinin plus recombinant interleukin-2-**activated peripheral blood lymphocytes** shows that mAb 8B4/20 identifies an antigen expressed on CD3+ cells by week 3 of culture. Thus, it recognizes a very late **activation** antigen (VLA) on mature T cells. The cell distribution and the electrophoretic pattern of the mol. identified by mAb 8B4/20 is distinct from that of known CD and of integrin/VLA mols. Its function on thymocytes is so far unknown; however, the **binding** of mAb 8B4/20 to **tumor** lines induces changes in the morphol. and adhesive properties of the 8B4/20+ cells growing in suspension. The authors suggest that mAb 8B4/20 recognizes a mol. that may be involved in interactions between thymocytes and other thymic structures that may be relevant for the selection process.

L6 ANSWER 8 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 7
AN 120:29024 CA
TI A majority of Ig H chain cDNA of normal human adult blood lymphocytes resembles cDNA for fetal Ig and natural autoantibodies
SO J. Immunol. (1993), 151(10), 5290-300
CODEN: JOIMA3; ISSN: 0022-1767
AU Huang, Chichi; Stollar, B. David
PY 1993
AB Certain Ig VH gene segments, with few or no mutations, recur frequently in natural autoantibodies, fetal **antibodies**, and products of **B cell tumors**. The goal of this study was to det. whether similar Ig gene segment usage occurs in normal human adult **PBL**. Extending previous analyses, 105 randomly picked H chain V region clones of representative cDNA libraries from **PBL** were sequenced. Clones were from: IgM and IgG libraries from one RNA sample of a normal adult; a second IgM library from the same subject 11 mo later; and one IgM library from a second subject. Although some clones had clear evidence of mutation, 48 of 77 IgM clones (62%) shared 99% or more identity with known germline VH segments, and most of these had no mutations in the CDR3 portion of the JH segment. Certain VH gene segments, expressed in autoantibodies and fetal **antibodies**, occurred at high frequency in these libraries. Fourteen of the clones with 99% identity to known VH segments had CDR3 segments identical to portions of known germline DH gene sequences; two such clones had no N nucleotides at the VHDH

or DHJH junctions. IgG-encoding sequences had more mutations than IgM-encoding sequences. JH and DH usage was not random. The circulating **B cell** population may represent a distinct compartment, with a large proportion of cells similar to those of the fetal and natural autoantibody repertoire. Polyreactive Ig products of these circulating cells may serve a screening function, **binding** and delivering diverse antigens (Ag) to secondary lymphoid tissues where more highly selective **antibodies** are formed to foreign or self-Ag.

L6 ANSWER 9 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 8
AN 119:223947 CA
TI **Tumor**-infiltrating lymphocytes derived from select **B-cell** lymphomas secrete granulocyte-macrophage colony-stimulating factor and **tumor** necrosis factor-.alpha. in response to autologus **tumor** stimulation
SO Blood (1993), 82(4), 1204-11
CODEN: BLOOAW; ISSN: 0006-4971
AU Schwartzentruber, Douglas J.; Stetler-Stevenson, Maryalice; Rosenberg, Steven A.; Topalian, Suzanne L.
PY 1993
AB **Tumor** infiltrating lymphocytes (TIL) were cultured from 17 **B-cell** lymphoma specimens derived from patients with predominantly low-grade malignancies. Specimens included 15 lymph-node biopsies, 1 malignant pleural effusion, and **PBL** from 1 patient with circulating lymphoma cells. The phenotypic and **proliferative** characteristics of TIL cultured in interleukin-2 (IL-2) were studied, as well as cytolysis and cytokine secretion in response to autologous **tumor**. Flow cytometry of fresh **tumor** suspensions showed that 50% of cells (median) were malignant **B cells** and 36% were infiltrating T lymphocytes. After culture for approx. 1 mo, TIL were 75% CD3+, 47% CD4+, and 35% CD8+. TIL **proliferation** was modest in most cases: the median max. expansion was 32-fold in 25 days. Lysis of autologous **tumor** in 4-h 51Cr release assays was mediated by 2 of 12 TIL studied, but was nonspecific. However, these same two TIL, when cocultured with various **tumor** stimulators, preferentially secreted **tumor** necrosis factor-.alpha. and granulocyte-macrophage colony-stimulating factor after autologous **tumor** stimulation; unstimulated TIL secreted undetectable or barely detectable levels of these cytokines. In one TIL culture, cytokines were secreted by purified CD4+ TIL but not by CD8+ cells, and secretion was completely abrogated by the anti-major histocompatibility complex (MHC) class II **antibody** IVA12. Thus, although specific cytokine secretion by lymphoma TIL in response to autologous **tumor** was obsd., it occurred in fewer than 20% of patients studied.

L6 ANSWER 10 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 9
AN 118:232248 CA
TI Epiligrin, a component of epithelial basement membranes, is an adhesive ligand for .alpha.3.beta.1 positive T lymphocytes

SO J. Cell Biol. (1993), 121(5), 1141-52
CODEN: JCLBA3; ISSN: 0021-9525
AU Wayner, Elizabeth A.; Gil, Susana G.; Murphy, George F.; Wilke, Mark S.; Carter, William G.
PY 1993
AB The cutaneous T cell lymphomas (CTCL), typified by mycosis fungoides, and several chronic T cell mediated dermatoses are characterized by the migration of T lymphocytes into the epidermis (epidermotropism). Alternatively, other types of cutaneous inflammation (malignant cutaneous **B cell** lymphoma, CBCL, or lymphocytoma cutis, non-malignant T or **B cell** type) do not show evidence of epidermotropism. This suggests that certain T lymphocyte subpopulations are able to interact with and penetrate the epidermal basement membrane. Here, T lymphocytes derived from patients with CTCL (HUT 78 or HUT 102 cells), adhere to the detergent-insol. extracellular matrix prepd. from cultured basal keratinocytes (HFK ECM). HUT cell adhesion to HFK ECM was inhibitable with monoclonal **antibodies** (mAbs) directed to the .alpha.3 (P1B5) or .beta.1 (P4C10) integrin receptors, and was up-regulated by an **activating** anti-.beta.1 mAb (P4G11). An inhibitory mAb, P3H9-2 raised against keratinocytes identified epiligrin as the ligand for .alpha.3.beta.1 pos. T cells in HFK ECM. Interestingly, 2 lymphocyte populations could be clearly distinguished relative to expression of .alpha.3.beta.1 by flow cytometry anal. Lymphokine **activated** killer cells, alloreactive cytotoxic T cells, and T cells derived from patients with CTCL expressed high levels of .alpha.3.beta.1 (.alpha.3.beta.1high). Non-adherent peripheral blood mononuclear cells, acute T or **B lymphocytic** leukemias, or non-cutaneous T or **B lymphocyte** cell lines expressed low levels of .alpha.3.beta.1 (.alpha.3.beta.1low). Resting **PBL** or .alpha.3.beta.1low T or **B cell** lines did not adhere to HFK ECM or purified epiligrin. However, adhesion to epiligrin was up-regulated by mAbs which **activate** the .beta.1 subunit indicating that .alpha.3.beta.1 activity is a function of expression and affinity. In skin derived from patients with graft-vs.-host (GVH) disease, exptl. induced delayed hypersensitivity reactions, and CTCL, the infiltrating T cells were stained with mAbs to .alpha.3 or .beta.1 and were localized in close proximity to the epiligrin-contg. basement membrane. Infiltrating lymphocytes in malignant cutaneous B disease (CBCL) did not express .alpha.3.beta.1 by immunohistochem. techniques and did not assoc. with the epidermal basement membrane. The present findings clearly define a function for .alpha.3.beta.1 in T cells and strongly suggest that .alpha.3.beta.1 interaction with epiligrin may be involved in the pathogenesis of cutaneous inflammation.

L6 ANSWER 11 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 10
AN 118:145520 CA
TI Melanoma cells and normal melanocytes share antigens recognized by HLA-A2-restricted cytotoxic T cell clones from melanoma patients
SO J. Exp. Med. (1993), 177(4), 989-98

CODEN: JEMEAV; ISSN: 0022-1007
AU Anichini, Andrea; Maccalli, Cristina; Mortarini, Roberta; Salvi, Stefania; Mazzocchi, Arabella; Squarcina, Paola; Herlyn, Meenhard; Parmiani, Giorgio
PY 1993
AB HLA-A2-restricted, CD3+, CD8+, .alpha./.beta.+ cytotoxic T cell (CTL) clones were isolated from peripheral blood (**PBL**) or **tumor** infiltrating lymphocytes (TIL) of two HLA-A2+ melanoma patients (9742 and 5810), to evaluate the possible recognition of autologous melanoma and of allogenic HLA-A2-matched normal melanocytes. These CTL clones lysed not only fresh and cultured autologous melanoma cells, but also allogeneic HLA-A2+, but not HLA-A2-, normal melanocytes. The lysis of autologous **neoplastic** cells and of melanocytes could be inhibited by an anti-HLA-A2 monoclonal **antibody** (mAb). Lysis of the normal melanocytes was not dependent on the presence of human or fetal calf serum in the culture medium. HLA-A2-restricted CTL clones recognized not only **proliferating** melanocytes cultured in complete melanocyte medium, but also melanocytes made quiescent by culture for up to 6 d in a basal medium devoid of exogenous factors such as phorbol ester (O-tetradecanoyl phorbol 13-acetate [TPA]), epidermal growth factor, insulin, and pituitary exts. Anal. of specificity of four CTL clones (A75, A83, A94, and 119) from patient 9742, performed on a panel of 39 targets, indicated that the three HLA-A2-restricted CTL (A75, A83, and A94) lysed all but one of nine allogeneic melanomas expressing the HLA-A2 mol. with no reactivity on nine HLA-A2- allogeneic melanomas. Only a few instances of borderline reactivity were seen by the same effectors on 21 targets of nonmelanocyte lineage, including 12 **carcinomas** of different histol., four Epstein-Barr virus-transformed **B cells** (lymphoblastoid cell lines [LCL]), including the autologous LCL, four lines of normal fibroblasts, and normal kidney cells. Lack of reactivity on allogeneic targets of nonmelanocyte lineage occurred in spite of expression of HLA-A2 on 14 of these targets as detd. by conventional tissue typing and cytofluorimetric anal. with four different anti-HLA-A2 mAb. These data indicate that tissue-related antigens can be expressed on normal and **neoplastic** cells of the melanocyte lineage and can be recognized in assocn. with HLA-A2 by CTL clones from melanoma patients.

L6 ANSWER 12 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 11
AN 120:132210 CA
TI CD30-antigen-specific targeting and **activation** of T cells via murine bispecific monoclonal **antibodies** against CD3 and CD28: potential use for the treatment of Hodgkin's lymphoma
SO Int. J. Cancer (1993), 54(5), 820-7
CODEN: IJCNAW; ISSN: 0020-7136
AU Pohl, Christoph; Denfeld, Ralf; Renner, Christoph; Jung, Wolfram; Bohlen, Heribert; Sahin, Ugur; Hombach, Andreas; van Lier, Rene; Schwonzen, Martin; et al.
PY 1993
AB Crosslinking of specific **tumor** antigens with the CD3 and

CD28 antigens can increase IL-2 secretion, **proliferation** and antigen-specific cytotoxicity in resting T cells. This crosslinking can be achieved effectively by bispecific monoclonal **antibodies** (BiMAb) with specificity for both the **tumor** antigen and CD3 or CD28 antigen, resp. BiMAb OKT3/HRS-3 with reactivity to both CD3 and the Hodgkin's-lymphoma-assocd. CD30 antigen and the BiMAb 15E8/HRS-3 with reactivity to both CD28 and CD30 antigen were generated by hybridoma fusion. Resting T cells were specifically **activated** to produce IL-2 by co-cultivation with a **B-cell** line only in the presence of the CD30/CD28 crosslinking BiMAb and an addnl. crosslinking anti-CD3/CD19 BiMAb. Neither the crosslinking BiMAbs alone nor any combination of the monospecific parental MAbs induced a comparable IL-2 prodn. by Jurkat cells in the presence of **B cells**. In addn., using a combination of these BiMAbs, an antigen-dependent cytotoxicity was induced by targeting APC-depleted **peripheral blood lymphocytes** to CD30+ L540 cells. T cells, previously specifically **activated** by CD3/CD30 in the presence of CD30 antigen, were cytotoxic to CD30+ cell lines only after incubation with BiMAb anti-CD28/CD30. Neither of the BiMAbs nor any of the parental **antibodies** induced a comparable effect.

L6 ANSWER 13 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 12
AN 120:132209 CA
TI Identification of colon-**tumor**-associated antigens by T-cell lines derived from **tumor**-infiltrating lymphocytes and **peripheral-blood lymphocytes** from patients immunized with an autologous **tumor**-cell/bacillus Calmette-Guerin vaccine
SO Int. J. Cancer (1993), 54(5), 734-40
CODEN: IJCNAW; ISSN: 0020-7136
AU Ransom, Janet H.; Pelle, Barbara A.; Hubers, Henk; Keynton, Linette M.; Hanna, Michael G. Jr.; Pomato, Nicholas
PY 1993
AB **Tumor** immunity developing as a response to an autologous colon-**tumor**/bacillus Calmette-Guerin (BCG) vaccine appears to be assocd. with induction of CD4+ helper T cells, implied by the observation that vaccine efficacy is assocd. with major histocompatibility complex class-II mol. expression on the vaccine **tumor** cells. Therefore, to identify colon-**tumor**-assocd. antigens responsible for conferring immunity, the authors examd. and compared the **proliferative** responses of **peripheral-blood lymphocytes** (**PBL**) from patients immunized with the autologous **tumor**/BCG vaccine to T-cell lines cloned expanded from colon-**tumor**-infiltrating lymphocytes to 5 antigens isolated on the basis of their reactivity by colon-**tumor**-reactive human monoclonal **antibodies**. Enzymically dissocd. colon **tumors** provided a source for establishment of cloned T-cell lines, **tumor** cell lines propagated in vitro or in vivo as nude-mouse xenografts and EBV-transformed **B-cell** lines used as antigen-presenting cells. Of

104 different T-cell lines tested, only 3 **proliferated** in response to CTAA 28A32-46K, and 1 to the CTAA 28A32-32K antigen. In contrast, **PBL** from 64% of patients immunized with the autologous colon-**tumor**/BCG vaccine responded to the CTAA 28A32-32K antigen. This antigen is related to a family of calcium- and phospholipid-**binding** placental proteins termed annexins. Since **proliferative** responses developed to this antigen after vaccination in 64% of individuals, this antigen may be an important common colon **tumor**-assocd. rejection antigen.

L6 ANSWER 14 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 13
AN 120:29016 CA
TI The B5 monoclonal human autoantibody **binds** to cell surface TNF.alpha. on human lymphoid cells and cell lines and appears to recognize a novel epitope. II
SO Cell. Immunol. (1993), 152(2), 569-81
CODEN: CLIMB8; ISSN: 0008-8749
AU Boyle, Petra; Lembach, Kenneth J.; Wetzel, Gayle D.
PY 1993
AB A human IgM monoclonal **antibody** (mAb) (B5) recognizing human **tumor** necrosis factor .alpha. (TNF.alpha.) was established from **peripheral blood lymphocytes** by transformation with Epstein-Barr virus and subsequent cell fusion. The B5 mAb **binds** to cell surface TNF.alpha. (csTNF.alpha.) on human T cells, **B cells**, and monocytes. In addn., this autoantibody **binds** to csTNF.alpha. on a variety of lymphoid and monocyte lineage cell lines of human origin, as well as astrocytomas, a breast **carcinoma**, and a melanoma. Interestingly, the B5 mAb also **binds** to chimpanzee lymphocytes and to mouse T lymphoma cell line csTNF.alpha.. Many neutralizing mouse anti-TNF.alpha. mAbs do not exhibit comparable **binding** to csTNF.alpha.. This is consistent with the previous demonstration that B5 recognizes an epitope on TNF.alpha. distinct from those recognized by three neutralizing mouse anti-TNF.alpha. mAbs. B5 **binding** to csTNF.alpha. is specific since it can be inhibited by TNF.alpha.. No inhibition of B5 **binding** was seen by a neutralizing mouse anti-TNF.alpha. mAb. The B5 autoantibody appears to recognize the transmembrane form of TNF.alpha. and most likely also recognizes TNF.alpha. assocd. with its receptor. The unique specificity of this B5 autoantibody provides some addnl. insight into the complex physiol. of cell surface-assocd. TNF.alpha..

L6 ANSWER 15 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 14
AN 120:161189 CA
TI Expression of membrane receptor for **tumor** necrosis factor on human blood lymphocytes
SO Immunol. Cell Biol. (1993), 71(4), 281-8
CODEN: ICBIEZ; ISSN: 0818-9641
AU Zola, H.; Flego, L.; Weedon, H.
PY 1993
AB Using a monoclonal **antibody** against the human p75

tumor necrosis factor receptor (TNFR-I) combined with a high-sensitivity immunofluorescence flow cytometric procedure, a proportion of **peripheral blood lymphocytes** can be shown to express TNFR-I constitutively. Approx. 50% of **peripheral blood lymphocytes** consisting mostly of CD4 cells and including most CD45R0-pos. cells, express TNFR-I. Receptor expression is increased by a variety of **activation** signals. Only a minority (.ltoreq.30%) of tonsil **B cells** express measurable levels of TNFR-I. The tonsil **B cells** which express TNFR-I include both cells with a germinal center cell phenotype and cells with the phenotype of the follicular mantle zone. **Activation** of **B cells** with anti-Ig, alone or in combination with interleukin-4 or interleukin-2, increases receptor expression, particularly in cells with the phenotype of mantle zone cells. The functional significance of constitutive expression of TNFR by blood and tissue lymphocytes is discussed.

L6 ANSWER 16 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 15
AN 118:122701 CA
TI Expression of surface lymphotoxin and **tumor** necrosis factor on **activated** T, B, and natural killer cells
SO J. Immunol. (1992), 149(12), 3881-8
CODEN: JOIMA3; ISSN: 0022-1767
AU Ware, Carl F.; Crowe, Paul D.; Grayson, Marcia H.; Androlewicz, Matthew J.; Browning, Jeffrey L.
PY 1992
AB The expression of membrane-assocd. forms of lymphotoxin (LT) and **tumor** necrosis factor (TNF) were examd. on cell lines of T, B, and myeloid origin; interleukin-2 (IL-2) dependent T cell clones; and **peripheral blood lymphocytes**. Inducible and constitutive patterns of surface LT expression were found on T cells as exemplified by the II-23.D7, a CD4+T cell hybridoma, and HUT-78, a T cell lymphoma. Phorbol ester induced surface LT expression on Ramos, an Epstein-Barr virus-transformed **B cell** line, but at a slower rate of appearance when compared to the II-23.D7. Secretion of LT was rapidly inducible by phorbol ester in II-23.D7 and also in HUT-78 but with slower kinetics; surface LT expression continued in both lines after secretion had ceased. Low levels of membrane TNF were transiently induced on II-23.D7 and HUT-78, but none was obsd. on Ramos. Peripheral blood monocytes and some myeloid **tumor** lines did not express surface LT. Several T cell clones expressed surface LT after antigen-specific stimulation, and expression persisted several days. Stimulation through the TCR or by IL-2 rapidly induced surface LT on resting peripheral T cells and CD56+ NK cells; pokeweed mitogen **activation** induced expression on CD20+ **B cells**. Consistent with previous results, immunopptn. with anti-LT monoclonal **antibody** showed that LT was complexed with a distinct 33-kDa glycoprotein (p33) on cells that expressed surface LT, whereas secreted LT was not assocd. with p33. Surface and secreted modes of LT expression by

activated T, B, and NK cells suggests that LT can be utilized as either a localized or diffusible mediator in immune responses.

L6 ANSWER 17 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 16
AN 118:57948 CA
TI Engraftment of human peripheral blood leukocytes into severe combined immunodeficient mice results in the long term and dynamic production of human xenoreactive **antibodies**
SO J. Immunol. (1992), 149(8), 2830-6
CODEN: JOIMA3; ISSN: 0022-1767
AU Williams, Scott S.; Umemoto, Takao; Kida, Hisashi; Repasky, Elizabeth A.; Bankert, Richard B.
PY 1992
AB Severe combined immunodeficient (SCID) mice engrafted with human peripheral blood leukocytes (hu-**PBL**-SCID) represent a potentially important small animal model for the study of human immune function. Attempts to generate human primary immune responses to exogenous antigen (Ag) in the hu-**PBL**-SCID have had limited success which raises questions about the functional capacity of human lymphocytes in the SCID environment. Here, it was demonstrated that the spontaneously secreted human Ig in hu-**PBL**-SCID includes **antibodies** with specificity for several different mouse RBC (mRBC) proteins. These **antibodies** apparently reflect the transfer of peripheral **B cells** which are responsible for the prodn. of naturally occurring xenoreactive **antibodies** in the donor. Western blot anal. showed that engraftment of anti-mRBC specificities was random among mice receiving **PBL** from the same donor sample. In at least one mouse, this engraftment was polyclonal and included human IgM and IgG which recognized at least 12 different mRBC proteins ranging in size from 35 to >200 kDa. Anti-mRBC specificities were found to vary with time demonstrating a dynamic expression of the human xenoreactive repertoire in hu-**PBL**-SCID. In contrast to mice engrafted with human **PBL**, mice engrafted with another source of human **B cells**, i.e., **tumor**-infiltrating leukocytes, produced very little or no human anti-mRBC **antibody**. Ag-driven **proliferation** of xenoreactive clones may result in a skewing of the engrafted human **B cells** in hu-**PBL**-SCID which could account in part for the limited ability of hu-**PBL**-SCID to respond to exogenous Ag. The long term prodn. of anti-mRBC **antibodies** and the modulation of the expressed xenoreactive repertoire obsd. in hu-**PBL**-SCID represents an opportunity to study the mol. genetics and cell biol. of the human humoral immune response to a defined complex Ag.

L6 ANSWER 18 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 17
AN 117:210462 CA
TI Production of natural killer cell stimulatory factor (interleukin 12) by peripheral blood mononuclear cells
SO J. Exp. Med. (1992), 176(5), 1387-98

CODEN: JEMEAV; ISSN: 0022-1007

AU D'Andrea, Annalisa; Rengaraju, Manthrasalam; Valiante, Nicholas M.; Chehimi, Jihed; Kubin, Marek; Aste, Miguel; Chan, Susan H.; Kobayashi, Michiko; Young, Deborah; et al.

PY 1992

AB Natural killer cell stimulatory factor (NKSF), or interleukin 12 (IL-12), is a 70-kD heterodimeric cytokine composed of two covalently linked chains, p40 and p35. NKSF/IL-12 has multiple effects on T and NK cells and was originally identified and purified from the supernatant fluid of Epstein-Barr virus (EBV)-transformed human **B lymphoblastoid** cell lines. The authors produced a panel of monoclonal **antibodies** against both chains of NKSF/IL-12. Some of these **antibodies** have neutralizing activity, and several combinations of them have been used to establish sensitive RIAs detecting the free p40 chain, the free p35 chain, or the p70 heterodimer. Using these reagents, it was detd. that most EBV-transformed human **B lymphoblastoid** cell lines constitutively produce low levels of the p70 heterodimer and an excess of the free p40 chain, whereas Burkitt lymphoma-derived, T, myeloid, and many solid **tumor**-derived cell lines produce neither. Prodn. of both p40 and p70 is increased several-fold upon stimulation of the EBV-transformed cell lines with phorbol diesters. The ability of supernatant fluids from unstimulated and phorbol diester-stimulated cell lines to induce interferon .gamma. (IFN-.gamma.) prodn. from T and NK cells, one of the effects of NKSF/IL-12, parallels the levels of prodn. of the p70 heterodimer, known to be the biol. active form of NKSF/IL-12. Staphylococcus aureus Cowan I strain (SAC) and other stimuli induce accumulation of p40 mRNA and prodn. of both p40 and p70 by peripheral blood mononuclear cells (PBMC). The producer cells appear to include both adherent cells and nonadherent lymphocytes, possibly **B cells**. The supernatant fluids from SAC-stimulated PBMC mediate the typical functions of NKSF/IL-12 (i.e., IFN-.gamma. induction, mitogenic effects on T/NK blasts, enhancement of NK cell cytotoxicity) at concns. of p70 similar to those at which recombinant NKSF/IL-12 mediates the same functions. Moreover, these activities are significantly inhibited by anti-NKSF/IL-12 **antibodies**. The neutralizing anti NKSF/IL-12 **antibodies** also inhibit 85% of the IFN-.gamma. prodn. in response to SAC, an NKSF/IL-12 inducer, and approx. 50% of the IFN-.gamma. prodn. in response to non-NKSF/IL-12-inducers such as IL-2, phytohemagglutinin, and anti-CD3 **antibodies**. These results indicate that induced or constitutively produced NKSF/IL-12 has a major role in facilitating IFN-.gamma. prodn. by **peripheral blood lymphocytes**. The findings that NKSF/IL-12 is both spontaneously produced and inducible in adherent PBMC and lymphocytes suggest that NKSF/IL-12 might be a major physiol. regulator of T and NK cell function during an immune response and inflammation.

L6 ANSWER 19 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 18

AN 115:181372 CA

TI **Tumor**-specific, cell surface-**binding** monoclonal

antibodies
SO PCT Int. Appl., 80 pp.
CODEN: PIXXD2
IN Freedman, Ralph S.; Ionnides, Constantin G.; Tomasovic, Barbara J.; Patenia, Rebecca S.
AI WO 90-US7496 901218
PI WO 9109135 A1 910627
PY 1991
AB A process is provided for the prepn. and use of gynecol. **tumor** diagnostic and **antitumor** agents. The process involves the pretreatment of a patient with a viral oncolyzate and the establishment of **B-cell** human hybridomas capable of producing human monoclonal **antibodies** (MAbs) reactive with cell-surface epitopes of human gynecol. **tumors**. Also disclosed are methods for using the MAbs in the diagnosis and treatment of gynecol. malignancies. Two esp. useful gynecol. hybridoma lines are disclosed which are derived from the process of the invention. Thus, cells from the lymph node of a patient with mucinous ovary **carcinoma** were fused with SPAZ4 cells (a heterohybridoma of mouse myeloma and human **peripheral blood lymphocytes**) using PEG 1500 to form the AC hybridoma cell line. The reactivity of human anti-ovarian surface-reacting MAb AC6C3 was tested with ovarian **carcinoma** cells and with a variety of nonovarian cell lines. MAb AC6C3 was also tested on cryostat sections of epithelial ovarian **carcinoma** specimens and compared to similar sections of other malignant as well as nonmalignant tissues. Immunopptn. with MAb AC6C3 identified a 32-kD band expressed on the surface of SKOV3 (ovarian **carcinoma**) cells.

L6 ANSWER 20 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 19
AN 115:253617 CA
TI A novel surface molecule expressed by long-term cultured T and natural killer cells is involved in cell **activation**
SO Eur. J. Immunol. (1991), 21(9), 1981-7
CODEN: EJIMAF; ISSN: 0014-2980
AU Ferrini, Silvano; Cantoni, Claudia; Ciccone, Ermanno; Biassoni, Roberto; Prigione, Ignazia; Bottino, Cristina; Venzano, Paola; Moretta, Lorenzo
PY 1991
AB Two monoclonal **antibodies** (mAb), termed ED6 and LD6, were obtained by immunizing mice with cytotoxic T cell lines expressing the T cell receptor (TcR) .gamma./.delta.. These mAb were selected according to their ability to trigger the cytolytic program of the immunizing cell lines in a redirected killing assay. Both mAb recognized mol.(s) expressed on the surface of most long-term cultured TcR .gamma./.delta.+, TcR .alpha./.beta.+ and CD3-CD16+ lymphocytes, while it was absent on resting **peripheral blood lymphocytes**. In addn. both mAb reacted with **neoplastic B cell** lines, Epstein-Barr virus-transformed **B cell** lines, small cell lung **cancer** and glioma cell lines, while no surface reactivity was detected on ovarian, breast, colon and non-small cell lung

cancer lines. The functional activity of these mAb was studied by two cytolytic assays. Both mAb were able to trigger the cytolytic program of CD3+TcR .gamma./.delta.+ polyclonal cell lines and of a CD3-CD16+ NK cell clone against the murine mastocytoma target cell line P815 (Fc receptor+) in a 4-h 51Cr-release assay. In addn., ED6 and LD6 hybridomas were lysed by TcR .gamma./.delta.+ effector cells while other hybridomas (obtained from the same fusion) were not lysed. ED6 and LD6 mAb (in the presence of submitogenic doses of the phorbol 12-myristate 13-acetate) also induced the secretion of interleukin 2 by ED6/LD6+ T cell clones expressing TcR .gamma./.delta. or .alpha./.beta.. MAb-induced surface antigen modulation expts. showed that the antigenic determinant recognized by ED6 and LD6 co-modulated, thus indicating that the two mAb probably recognized the same or closely assocd. mols. The mol. characteristics of the antigen recognized by the mAb were investigated by Western blot anal. The LD6 mAb recognized a major band of approx. 65 kDa, both under nonreducing and reducing conditions. These data indicate that ED6 and LD6 mAb recognize a novel non-lineage-specific **activation** antigen which is involved in the induction of the functional program of long-term Tor natural killer cells.

L6 ANSWER 21 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 20
AN 115:205678 CA
TI Characterization of normal human lung lymphocytes and interleukin-2-induced lung T cell lines
SO Am. J. Respir. Cell Mol. Biol. (1990), 3(5), 441-8
CODEN: AJRBEL; ISSN: 1044-1549
AU Becker, Susanne; Harris, David T.; Koren, Hillel S.
PY 1990
AB Lymphocytes from the lower respiratory tract were obtained by bronchoalveolar lavage of healthy, non-smoking individuals. Various monoclonal **antibodies** characterizing **activated** T cells, helper-inducer and suppressor-inducer T cell subsets, and naive vs. memory cells were used to define the phenotype of these lymphocytes. The highly variable CD4/CD8 ratio and the large proportion of the T cells expressing HLA-DR suggested that the T cells were recently **activated** by antigens selectively stimulating either helper or cytotoxic/suppressor T cell function. Indeed, the CD45RA antigen, a marker characteristic of suppressor-inducer T cells when coexpressed with CD4, and naive T cells in general, was absent from T cells in most prepns., while the CD45RO antigen, a marker of memory cells and immature thymocytes, was present on 68 to 100% of all lung T cells. The majority (>70%) of the CD4+ helper T cells was CD45RO+ CD45RA-, a phenotype found on T cells that provide help for **B cell** Ig synthesis. Lung T cells **proliferated** poorly in response to phytohemagglutinin and Con A but did respond to **activation** with low concns. of anti-CD3 mAb (2 to 25 ng/mL) and to interleukin-2 (IL-2) alone to similar extent as did autologous **peripheral blood lymphocytes** . Stimulation of lung T cells having a CD4/CD8 ratio of >2 with IL-2 (100 U/mL) resulted in outgrowth of helper T cell lines (CD2,

CD3, CD4, TCR.alpha./.beta., CD45RO) with no cytotoxic activity against K562 **tumor** target cells. In contrast, stimulation of cell prepns. with a CD4/CD8 ratio <2 resulted in T cell lines with low cytotoxic activity against K562 cells. These latter lines contained >40% CD8+ cells, all of which expressed the TCR.alpha./.beta.. Cytotoxic activity did not correlate with expression of natural killer (NK) antigen CD56 (Leu19). Helper cell lines were maintained for at least 3 mo in culture, while cytotoxic cell lines **proliferated** for <6 wk. These data show that the lower respiratory tract of humans contains immunocompetent lymphocytes that may have been recently **activated** and are long-lived memory cells of either the helper or the cytotoxic/suppressor cell type, both of which are capable of **proliferation** in response to appropriate stimulation (anti-CD3 mAb or IL-2).

L6 ANSWER 22 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 21
AN 114:30001 CA
TI Selectivity of **antibody**-targeted anthracycline antibiotics on T lymphocytes
SO J. Bioact. Compat. Polym. (1990), 5(3), 249-66
CODEN: JBCPEV; ISSN: 0883-9115
AU Rihova, Blanka; Strohalm, Jiri; Plocova, Dana; Ulbrich, Karel
PY 1990
AB Targeted polymeric prodrugs based on N-(2-hydroxypropyl)methacrylamide (HPMA) were tested on human **peripheral blood lymphocytes** or mouse splenocytes triggered in vitro to **proliferation** by T cell specific (Con A) or **B cell** specific (Staphylococcus aureus Cowan I) mitogens. Only a selective inhibition of 3H-thymidine incorporation by T lymphocytes was obsd. after in vitro incubation with prodrugs prepd. by covalent attachment of daunomycin or adriamycin and **antibody** (anti-CD3; anti-Thy 1.2) to biodegradable oligopeptide side chains of sol. synthetic copolymer HPMA. The in vitro results were confirmed in vivo by inhibition of **antibody** response to thymus dependent (ARS-BGG) or thymus independent (TNP-E. coli) antigens in normal and in athymic mice. After administration of biocompatible, **antibody** targeted prodrugs only the **antibody** response against ARS-BGG was considerably reduced.

L6 ANSWER 23 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 22
AN 111:192755 CA
TI Synergistic **antitumor** effects of interleukin 2 and the monoclonal Lym-1 against human Burkitt lymphoma cells in vitro and in vivo
SO Cancer Res. (1989), 49(19), 5377-9
CODEN: CNREA8; ISSN: 0008-5472
AU Gill, Indrani; Agah, Ravin; Hu, Eddie; Mazumder, Amitabha
PY 1989
AB Interleukin 2 (IL-2) regulates immune responses by inducing **proliferation** and differentiation of T-cells into cytotoxic cells, inducing lymphokine **activated** killer activity and

enhancing **antibody** dependent cellular cytotoxicity (ADCC). Lym-1, a monoclonal **antibody**, recognizes a membrane antigen present on the surface of **B-lymphoma** cells and can be used for ADCC. The authors therefore used Raji (human Burkitt lymphoma) cells to study the efficacy of combination therapy with IL-2 had a synergistic **antitumor** effect. The max. synergism was achieved when **peripheral blood lymphocytes** were incubated with IL-2 for 3 days as compared to 1 or 2 days, with the optimal concn. of IL-2 being 1000 units/mL. This effect was specific for Lym-1 as demonstrated by expts. using an irrelevant (antimelanoma) monoclonal **antibody** or an irrelevant target cell (A375). The ADCC was blocked by an anti-Fe receptor **antibody** (3G8). In vivo expts. performed by growing Raji **tumors** in nude mice also demonstrated the increase in ADAcC and the synergism between IL-2 and Lym-1 in terms of decreased **tumor** size and growth. The mechanism of this synergy is probably from **activation** of cells mediating ADCC. This raises the possibility that treatment of patients with low doses of IL-2 in combination with Lym-1 may enhance immune responses and thereby **antitumor** activity.

L6 ANSWER 24 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 23
AN 112:34166 CA
TI A monoclonal **antibody**, H2, defines a new surface antigen expressed on human lymphocytes
SO Scand. J. Immunol. (1989), 30(5), 573-81
CODEN: SJIMAX; ISSN: 0300-9475
AU Grunewald, J.; Janson, Carl Harald; Tehrani, M. J.; Porwit, A.; Matsuo, Y.; Mellstedt, H.; Wigzell, H.
PY 1989
AB A monoclonal **antibody** (MoAb), H2, was previously described which recognized a **tumor**-unique antigen on a human T-cell chronic lymphatic leukemia (T-CLL, CD3,4+). However, further characterization of H2 has revealed a reactivity with the majority of T lymphocytes and a minority of **B lymphocytes**, some malignant T cells, and a few cell lines of leukemia or of hematopoietic **tumor** origin. The mol. wt. of the antigen (80,000) pptd. by the MoAb H2 from the cell lines NALM-6 and Reh corresponded to that previously found. When **PBL** were stimulated with PHA, IL-2, or Con A a reduced reactivity of H2 could be seen. The MoAb H2 was submitted to the Fourth International Conference on Human Leukocyte Differentiation Antigens, Vienna, 1989. H2 did not cluster in any of the 78 clusters of differentiation (CD 1-78) discussed at the conference, indicating its unique reactivity. Thus, a new antigen was defined on lymphocytes with a possible role along the resting-**proliferating** axis.

L6 ANSWER 25 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 24
AN 112:19676 CA
TI Persistent superphosphorylation of leukosialin (CD43) in **activated** T cells and in **tumor** cell lines
SO Scand. J. Immunol. (1989), 30(5), 539-47

CODEN: SJIMAX; ISSN: 0300-9475
AU Axelsson, Brent; Perlmann, P.
PY 1989
AB CD43 (leukosialin) is a highly sialylated, single-chain mol. expressed on most human leukocytes. Regulatory signals appear to be transduced through the mol. as suggested by the ability of anti-CD43 **antibodies** to induce aggregation and **proliferation** of T cells and to enhance **B-cell proliferation** and natural killer cell activity. **Activation** of protein kinases is an essential event in signal transduction. It was studied whether CD43 may function as a substrate for protein kinases during mitogenic **activation** of lymphocytes. CD43 was rapidly superphosphorylated (within minutes) on serine residues following addn. of phorbol ester (PMA) to **peripheral blood lymphocytes**. PMA treatment of the cells was not followed by rapid down-regulation of CD43. **Activation** of the lymphocytes by Con A or anti-CD3 **antibodies** (OKT-3) also resulted in superphosphorylation of CD43. However, the phosphorylation was delayed as compared to that induced by PMA and was detected 3-4 h after the addn. of the reagents. A plateau was reached after 24-48 h of stimulation. Interestingly, the high level of phosphorylation of CD43 was maintained in long-term cultures of T cells **activated** by various means. Furthermore, CD43 was constitutively superphosphorylated (on serine and tyrosine) in continuously growing cell lines of T, B, and non-lymphoid origin. Thus, CD43 has an important role during both early and late phases of T-cell **activation** and modulation of its biochem. properties by protein kinases may be assocd. with progression through the cell cycle and with cellular growth.

L6 ANSWER 26 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 25
AN 111:37739 CA
TI Expression of low-affinity receptor for IgE (Fc.epsilon.RII, CD23) and IgE-BF (soluble CD23) release by lymphoblastoid **B-cell** line RPMI-8866 and human peripheral lymphocytes of normal and atopic donors
SO Immunology (1989), 66(4), 505-11
CODEN: IMMUAM; ISSN: 0019-2805
AU Bujanowski-Weber, J.; Brings, B.; Knoeller, I.; Pfeil, T.; Koenig, W.
PY 1989
AB The low-affinity receptor for IgE (CD23) as well as the sol. IgE-**binding** factors (IgE-BF, sCD23) are important factors in IgE **antibody** regulation. The CD23 expression and the concomitant release of CD23 were analyzed from the lymphoblastoid **B-cell** line RPMI-8866 and from **peripheral blood lymphocytes** (**PBL**) of healthy volunteers as well as atopic patients. CD23 expression and sCD23 release of RPMI-8866 cells were dependent on the stage of culture. While CD23 expression decreased with increasing time of culture (day 1-3), the sCD23 release was enhanced during the culture period. Cytokines such as interleukin (IL)-4, IL-2, **tumor** necrosis

factor .alpha., and interferon-.alpha. exerted various effects on the target cells depending on the culture period. CD23 expression on normal lymphocytes was lower compared with the expression on atopic cells. Lymphokines (IL-2, IL-4) as well as mitogens (PHA, Con A) enhanced CD23 expression and IgE-BF (sCD23) release. The degree of enhancement was always higher with atopic cells compared with the results obtained with cells of normal donors.

L6 ANSWER 27 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 26
AN 108:110711 CA
TI Lymphokine-**activated** killer cells in rats: analysis of progenitor and effector cell phenotype and relationship to natural killer cells
SO Cancer Res. (1988), 48(4), 884-90
CODEN: CNREA8; ISSN: 0008-5472
AU Vujanovic, Nikola L.; Herberman, Ronald B.; Olszowy, Michael W.; Cramer, Donald V.; Salup, Raoul R.; Reynolds, Craig W.; Hiserodt, John C.
PY 1988
AB The progenitor and effector cell phenotype of lymphokine-**activated** killer (LAK) cells generated in F344 rats by recombinant human interleukin 2 (rIL-2) were analyzed. Highly purified populations of peripheral blood large granular lymphocytes (LGL) exhaustively depleted of T-cells were fully capable of generating high levels of LAK activity by 3-5 days in culture while purified populations of resting T-cells devoid of LGL could not generate LAK activity. This pure population of LGL expressed surface markers characteristic of rat natural killer (NK) cells. Further evidence that NK cells were the progenitors of cells with LAK activity was obtained by treatment of spleen or **peripheral blood lymphocytes** with anti-laminin or anti-asialo-GM1 **antibodies** plus complement or with the lysosomotropic agent L-leucine Me ester. These treatments effectively depleted LGL/NK cell activity and the subsequent generation of rIL-2-induced LAK activity. Anal. of the LAK effector phenotype by cell sorting demonstrated that the majority of cells with LAK activity were also LGL and expressed surface marker characteristic of **activated** NK cells and not those of mature T- or **B-cells**. Thus, in the rat, the major cell population **activated** by rIL-2 is the LGL/NK cell and these cells appear to represent the major population of cells in blood or spleen which generate broad **antitumor** (LAK) cytotoxicity.

L6 ANSWER 28 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 27
AN 110:93301 CA
TI Characterization of human CD4+ T-cell clones that secrete helper factor(s) for **B-cell proliferation** and maturation
SO Scand. J. Immunol. (1988), 28(5), 519-27
CODEN: SJIMAX; ISSN: 0300-9475
AU Berzins, T.; Varegas-Cortes, M.; Axeelsson, B.; Hammarstrom, M. L.; Hammarstroem, S.; Perlmann, P.

PY 1988
AB Human **peripheral blood lymphocytes** (**PBL**) were **activated** with K46M, a mitogenic monoclonal **antibody** against La-reactive T lymphocyte surface structures. The cultures were expanded in the presence of interleukin 2 (IL-2). After 1 mo of culture, the **activated** T cells were cloned by limiting diln. at 0.5 cells/well. Five clones with the CD3+CD4+ phenotype and one clone with the CD3+CD8+ phenotype were obtained. The CD3+CD8+ clone (K99) displayed a strong major histocompatibility complex (MHC)-unrestricted cytolytic activity against MOLT-4 and a weaker reactivity against the bladder **tumor** cell lines T24 and RT4. The natural killer (NK)-susceptible K562 cells were not lysed. Two of the CD3+CD4+ clones (K91 and K914) showed a helper activity in pokeweed mitogen (PWM)-induced IgG prodn. by **B cells**. These cells differed in the expression of CD45R and CDw29 antigens. When stimulated with PWM for 48 or 72 h, clone K91 and an addnl. CD4-pos. clone (K913) secreted a factor into the supernatants which helped **B cells** to produce IgG. The K913 supernatant also induced some IgM prodn. The supernatant obtained after similar stimulation of K914 cells was inactive. None of these supernatants induced **B cells** to **proliferate** when tested together with phorbol myristate acetate. However, when K91 and K914 cells were **activated** with phytohemagglutinin (PHA) for 48 or 72 h, the supernatant from K91 was strongly helpful in **B-cell proliferation**, whereas the supernatant from K914 cultures was only moderately active. Thus, human T helper clones were established that release different factors supporting either **B-cell proliferation** or maturation when stimulated with PWM or PHA.

L6 ANSWER 29 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 28
AN 109:36346 CA
TI Leukemia-differentiating activity expressed by the human melanoma cell line LD-1
SO Leuk. Res. (1988), 12(3), 217-25
CODEN: LEREDD; ISSN: 0145-2126
AU Lilly, Michael B.; Kraft, Andrew S.
PY 1988
AB A leukemia-differentiating activity (LDA) was identified in medium conditioned by the LD-1 melanoma, a granulocyte-colony-stimulating factor (G-CSF)-secreting human **tumor** line. Partially-purified LDA induces HL-60 cells to produce superoxide, become phagocytic, and to develop macrophage-like morphol. and surface markers. The LDA markedly suppresses clonal growth in agar of HL-60 cells, and cells of the human myeloid leukemia lines **PBL** 985 and K562, but does not suppress clonal growth of the **B-lymphoblast** lines Raji and Daudi. The mol. wt. of this material is approx. 40,000 daltons. It can be sepd. from the bulk of the colony-stimulating activity on Ph sepharose chromatog. The LDA is not neutralized by **antibodies** to G-CSF, granulocyte-macrophage CSF, interferon-.alpha. or -.gamma., **tumor** necrosis factor, urokinase, and tissue plasminogen

activator, and is not inhibited by preincubation with aprotinin. The LDA in conditioned medium may be different from previously described differentiating factors, and may represent an addnl. class of human growth regulators.

L6 ANSWER 30 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 29
AN 107:234604 CA
TI Immortalization of human lymphocytes from a **tumor**-involved lymph node
SO Cancer Res. (1987), 47(19), 5181-8
CODEN: CNREA8; ISSN: 0008-5472
AU Glassy, Mark C.
PY 1987
AB Lymphocytes isolated from a regional draining lymph node of a patient with a **carcinoma** of the vulva were fused with human UC729-6 cells. The generated human-human hybridomas were tetraploid with the 21p+ chromosomal marker of UC 729-68, expressed HLA derived from the patient's cells, and have been stable in culture for 2 yr. Supernatants from 6 IgG-secreting hybridomas had broad reactivity profiles with human **carcinoma** cells and no reactivity with hematopoietic cell lines (B- and T-cells, myelomas, leukemias, lymphomas), red blood cells, **peripheral blood lymphocytes**, and normal fibroblasts. All 6 human IgG monoclonal **antibodies** reacted with the A431 cell line, an epidermoid **carcinoma** of the vulva, similar to the patient's **cancer**. The supernatant of one hybridoma, which phenotyped as having T-cell parentage, enhanced the cloning efficiency of human hybrids, suggesting the presence of a growth factor(s). In serum-supplemented cultures these hybrids secreted 200 ng to 3 .mu.g of IgG/mL/106 cells/24 h and in serum-free medium, an enhanced prodn. of 1-9 .mu.g of IgG/mL/106 cells/24 h. One IgG monoclonal **antibody**, VLN3G2, pptd. a single chain protein with an apparent mol. wt. of 48,000 from Nonidet P-40 exts. of A431 cells. Apparently, regional draining lymph nodes of **cancer** patients are highly immunoreactive and contain **B-cells** whose Ig recognizes putative **tumor**-assocd. antigens.

L6 ANSWER 31 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 30
AN 106:143861 CA
TI Selective killing of T lymphocytes by phototoxic liposomes
SO Proc. Natl. Acad. Sci. U. S. A. (1987), 84(1), 246-50
CODEN: PNASA6; ISSN: 0027-8424
AU Yemul, Shrishailam; Berger, Carole; Estabrook, Alison; Suarez, Sylvia; Edelson, Richard; Bayley, Hagan
PY 1987
AB Two-fold specificity in drug delivery obtained through the localized **activation** of drugs by phys. means and the attachment of drugs to proteins that **bind** to target cells might be used for highly selective **cancer** chemotherapy or for immunosuppression. Toward this end, a monoclonal **antibody** against an antigen on the surface of T lymphocytes was covalently attached to liposomes contg. a phototoxic drug, pyrene [129-00-0],

bound to the lipid bilayer. When unfractionated **peripheral blood lymphocytes**, or B- and T-cell lines, were irradiated after treatment with these liposomes, T cells were killed while **B cells** were spared, demonstrating the validity of the approach in a simple in vitro assay.

L6 ANSWER 32 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 31
AN 106:136581 CA
TI Distribution and functional analysis of a 120- to 130-kDa T-cell surface antigen
SO Cell. Immunol. (1987), 105(1), 161-73
CODEN: CLIMB8; ISSN: 0008-8749
AU Yssel, Hans; De Vries, Jan E.; Borst, Jannie; Spits, Hergen
PY 1987
AB A monoclonal **antibody** (mAb), SPV-L14, was raised that detected a human T-cell surface antigen with a mol. wt. (MW) of 120 kilodaltons (kDa) on resting and PHA-**activated** peripheral blood T lymphocytes (**PBL**). An addnl. band with a MW of 130 kDa could be pptd. with variable intensities from thymocytes, **neoplastic** T cells, and CD4+- or CD8+ T-cell clones. Based on their reactivity with SPV-L14 and a mAb directed against CD3, 4 subpopulations of CD2+ lymphocytes were detected and their existence was confirmed at the clonal level. The majority (95%) of the CD3+ cells were SPV-L14+, whereas 5% were CD3+, SPV-L14-. Among cloned cell lines CD3-, SPV-L14- and CD3-, SPV-L14+ cells were found to exist. The CD3-, SPV-L14- and CD3-, SPV-L14+ clones had natural killer (NK) cell activity, indicating that the 120-130-kDa antigen is expressed heterogeneously on CD3- NK cell clones. In addn., **neoplastic** T cells representing these 4 subpopulations were shown to exist. Although the tissue distribution and the MW of the SPV-L14 target antigen strongly suggest that SPV-L14 reacts with an epitope on CD6, the SPV-L14 mAb did not react with resting or **activated B cells** or with malignant **B cells**. Blocking studies showed that SPV-L14 inhibited the **proliferative** response of **PBL**, induced by anti-CD3 mAb, but that SPV-L14 did not affect the **proliferation** induced by PHA. Apparently, the 120-130-kDa MW antigen is assocd. with T-cell **proliferation**, depending on the mode of **activation**.

L6 ANSWER 33 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 32
AN 105:59243 CA
TI Suppression of polyclonal immunoglobulin production by a soluble factor produced by a human thymus hybridoma
SO Immunopharmacology (1986), 11(3), 141-54
CODEN: IMMUDP; ISSN: 0162-3109
AU Murakami, Masato; Cathcart, Martha K.
PY 1986
AB A human thymus cell hybridoma was established by using thymus cells obtained from a patient with common variable hypogammaglobulinemia and assocd. thymoma. This hybridoma secreted a suppressor factor for polyclonal **antibody** synthesis. Supernatants of this

hybrid showed 40-80% suppression of both IgM and IgG synthesis by pokeweed mitogen-stimulated human **peripheral blood lymphocytes**. Hybridoma supernatants were suppressive for Ig prodn. only if added within the initial 48 h of the 7-day culture period. Suppression of **antibody** prodn. by the hybridoma supernatant was prevented by preabsorption with T lymphocytes. Further, the suppressor factor inhibits **antibody** prodn. in reconstructed cultures contg. T4+ cells and **B cells**, yet the suppression could be abrogated by increasing the no. of T4+ cells. The hybrid supernatant had no affect on the **proliferation** of human mononuclear cells in response to pokeweed mitogen, lipopolysaccharide, concanavalin A or alloantigen but inhibited phytohemagglutinin-induced **proliferation**. The target cell population for the inhibition of phytohemagglutinin responsiveness was a T4+ lymphocyte (helper inducer T cell). These results suggest that thymus hybridoma cells can produce immunoregulatory products that act through the modulation of T4+ lymphocyte function. This is the first human thymus cell hybridoma to be reported. Studies on such cell lines may provide important information on immunoregulatory thymic factors.

L6 ANSWER 34 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 33
AN 104:107780 CA
TI Leukoregulin, an **antitumor** lymphokine, and its therapeutic uses
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
IN Ransom, Janet H.; Mccabe, Richard P.; Haspel, Martin V.; Pomato, Nicholas
AI WO 85-US626 850411
PI WO 8504662 A1 851024
PY 1985
AB A unique human lymphokine, designated leukoregulin because it is a leukocyte product and a cell growth regulatory substance that is molecularly and biol. distinct from other known lymphokines, was isolated and characterized. Leukoregulin has the ability to inhibit the growth of human **tumor** cells by direct lysis, inhibit cellular **proliferation**, and enhance natural killer (NK) cell-mediated destruction. It has a mol. wt. of .apprx.120,000-140,000 with subunits on dissocn. of .apprx.30,000-35,000 daltons. Leukoregulin was isolated from human peripheral blood leukocytes (**PBL**) by conventional methods. Leukoregulin formation was enhanced by exposure of **PBL** to phytohemagglutinin or TPA. Human **B-cell** lines and hybridomas that secreted leukoregulin and monoclonal **antibodies** to cell surface receptors for leukoregulin were prepd. A method for cloning the leukoregulin gene was outlined.

L6 ANSWER 35 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 34
AN 102:147328 CA
TI Pokeweed mitogen-induced immunoglobulin secretion by **peripheral blood lymphocytes** from patients with primary intracranial **tumors**.

Characterization of T helper and **B cell** function
SO J. Immunol. (1985), 134(3), 1545-50
CODEN: JOIMA3; ISSN: 0022-1767
AU Roszman, Thomas L.; Brooks, William H.; Steele, Charlene; Elliott, Lucinda H.
PY 1985
AB Patients with primary malignant brain **tumors** have impaired in vivo and in vitro cell-mediated immunity. Pokeweed mitogen (PWM)-induced secretion of Ig by **peripheral blood lymphocytes** (**PBL**) was used to further investigate impaired lymphocyte function in these patients. The PWM response of **PBL** from normal individuals averaged 8384 plaque-forming cells (PFC)/106 cells, whereas the response of **PBL** from patients averaged 1590 PFC/106. The decreased PWM response of **PBL** patients could not be improved by varying the no. of **PBL** placed in culture or employing different concns. of PWM. Co-culture expts. to detect the presence of suppressor cells in **PBL** and purified T cell prepns. from patients demonstrated that enhanced suppressor cell activity was not evident. Next, expts. were performed to assess the T-helper cell activity present in purified T cell prepns. obtained from patients. The results demonstrated that T cells from patients lacked the ability to provide adequate helper activity in the PWM response. Moreover, studies with monoclonal **antibodies** directed against T cell subsets revealed that **PBL** from patients have a reduced percentage of T-helper cells (40%) as compared with normal values (55%). In concert with T-helper cell anomalies, **B cell** function in these patients also is diminished. Thus, a combined T-helper and **B cell** defect may contribute to the broad impairment of host immunocompetence obsd. in patients with primary gliomas.

L6 ANSWER 36 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 35
AN 97:37240 CA
TI Structural characterization of the human T cell surface antigen (p67) isolated from normal and **neoplastic** lymphocytes
SO J. Immunol. (1982), 129(1), 401-5
CODEN: JOIMA3; ISSN: 0022-1767
AU Fox, Robert I.; Harlow, Darla; Royston, Ivor; Elder, John
PY 1982
AB A 67,000-dalton glycoprotein (p67) on normal and **neoplastic** T cells is defined by reactivity with a monoclonal **antibody** (**antibody** SC1) derived against human T chronic lymphocytic leukemia (T-CLL) cells. This antigen is present on >90% of normal thymocytes, normal peripheral blood (**PBL**) T cells, T acute lymphoblastic leukemia (T-ALL), T-CLL, and **B cell** chronic lymphocytic leukemia (B-CLL). It is absent from normal **B cells**, **B cell** lines, myeloid cells, and stem cell precursors. By using immunopptn. of 125I-labeled glycoproteins and chymotrypsin digestion, the peptide maps of p67 from normal and leukemic lymphocytes revealed that the antigen is highly related among these cell sources, but at least 2 major forms of the mol. could be identified. One form was prevalent

on the T-ALL-derived cell line 8402 and a second form on cell line HPB-T ALL. Peptide maps of **PBL** from a normal patient, from a T-ALL patient, and from a B-CLL patient were similar to HPB-T ALL cells. In addn. to the 2 major forms of p67, subtle shifts in certain peptides were noted in lymphocytes from each source. The peptide fingerprints of p67 were similar to those obtained from murine Lyt-1 antigen, suggesting possible homol., and were distinctly different from those of murine gp70. Sequential immunopptn. expts. verified that the p67 antigen is carried on the same mol. recognized by other independently derived monoclonal **antibodies** including SC1, L1F12, T101, and OKT1. Cross-blocking expts. indicated that preincubation with **antibody** L17F12 or T101, but not OKT1, could block subsequent **binding** of biotin-conjugated **antibody** SC1. Thus, 4 of 5 monoclonal **antibodies** derived by sep. immunizations recognize identical or closely located antigenic sites on p67.

L6 ANSWER 37 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 36
AN 95:201711 CA
TI cAMP receptor proteins and protein kinases in human lymphocytes: fundamental alterations in chronic lymphocytic leukemia cells
SO Eur. J. Biochem. (1981), 120(3), 585-92
CODEN: EJBCAI; ISSN: 0014-2956
AU Weber, Wolfgang; Schwoch, Gerhild; Wielckens, Klaus; Gartemann, Axel; Hilz, Helmuth
PY 1981
AB To study the significance of cAMP receptor proteins and protein kinase activities in **tumor** dedifferentiation, **peripheral blood lymphocytes** from normal donors and from patients with chronic lymphocytic leukemia were studied. Both normal and **tumor** lymphocyte populations were devoid of cell **proliferation**. Normal human lymphocytes contained about equal activities of histone kinase and casein kinase. Of the total histone kinase, cAMP-dependent activity in normal and **tumor** lymphocytes comprised about 50% as shown by the use of the heat-stable inhibitor. The **tumor** lymphocytes, however, exhibited decreased values of all 3 protein kinase activities, the most pronounced decrease (to 7% of the normal control cells) being obsd. with the casein kinase. Total high-affinity cAMP-**binding** sites (= regulatory subunits R of cAMP-dependent protein kinase type I and II) in leukemic lymphocytes were also reduced (to <20%). Immunotitration with specific **antibodies** raised against rabbit muscle RI and bovine heart RII showed that about 60% of the cAMP-**binding** sites were assocd. with type RI regulatory subunits in both normal and leukemic lymphocytes. Immunoreactive RII components comprised about 40% of total **binding** sites in lymphocytes of chronic lymphocytic leukemia, but only 20% in normal cells, the residual 20% being represented by RI protein of low immunoreactivity. Combination of gel electrophoretic anal. of the cAMP-**binding** protein labeled with [32P]n3cAMP and **binding** to the R-specific **antibodies** allowed the identification of

individual type I and type II R proteins. Besides the regulatory subunit RI of 49 kilodaltons present in both cell types, addnl. isoproteins were found, the predominant RII form being a 52 kilodalton subunit in leukemic lymphocytes. The findings in lymphocytes of chronic lymphocytic leukemia cannot be explained by the fact that they are B-type lymphocytes. Control expts. revealed that normal **B lymphocytes** do not differ significantly from total blood lymphocytes with respect to the parameters mentioned. Biochem. correlates of the dedifferentiated status of these nonproliferating (G0) cells from patients with chronic lymphocytic leukemia, then, are represented by reduced levels of protein kinases and of basal cAMP and to the state of differentiation, independently from cell **proliferation.**

L6 ANSWER 38 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 37
AN 96:50491 CA
TI Alpha-fetoprotein on human **peripheral blood lymphocytes** does not block complement-dependent lymphocytotoxicity
SO Scand. J. Immunol. (1981), 14(3), 309-13
CODEN: SJIMAX; ISSN: 0300-9475
AU Ren, E. C.; Chan, S. H.
PY 1981
AB Using a direct immunofluorescence assay, it was shown .alpha.-fetoprotein (AFP) both in purified form and in hepatocellular **carcinoma** (HCC) sera was capable of **binding** onto 10-20% of T lymphocytes and 5-10% of **B lymphocytes** in human peripheral blood when these lymphocytes were preincubated in AFP-pos. fluids at 4.degree. in the presence of sodium azide. But when the preincubation temp. was raised to 37.degree., most of the membrane-**bound** AFP was internalized or shed, and, consequently, <3% of the cells showed pos. membrane fluorescence. In addn., **binding** of AFP onto lymphocyte surface membrane and the continuous presence of large amts. of AFP in these lymphocyte cultures did not interfere with the action of cytotoxic **antibodies** directed against HLA determinants on the lymphocyte surface.

L6 ANSWER 39 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 38
AN 96:157095 CA
TI Effects of a **tumor** promoter, 12-O-tetradecanoylphorbol 13-acetate (TPA), on human **peripheral blood lymphocytes**: induction of suppressor T cells and reduction of natural killing (NK) and **antibody**-dependent cellular cytotoxicity (ADCC)
SO Mie Med. J. (1981), 31(1), 37-52
CODEN: MMJJAI; ISSN: 0026-3532
AU Hirata, Hiroshi
PY 1981
AB 12-O-tetradecanoylphorbol 13-acetate (TPA)(I) [16561-29-8] proved to be a potent mitogen for human **peripheral blood lymphocytes** both thymus-derived (T) cells and bone marrow-derived (B) **cells**, and inhibited the DNA

synthesis in a 1-way mixed lymphocyte response. TPA-**activated** T cells also markedly suppressed the **proliferative** responses of autologous T and **B cells** to mitogens and allogeneic cells. The supernatant of TPA-**activated** T cells had the same degree of suppressor capability as TPA-**activated** T cells. TPA also increased IgG-Fc receptor-bearing T cells and autologous erythrocyte rosette-forming T cells. Therefore, TPA induced the suppressor effector T cells or the T cell subsets that are required for the expression of suppressor activity, such as suppressor precursor or amplifier T cells. In addn., TPA reversely reduced NK and ADCC activities by active suppression of the effectiveness of NK and K cells. Thus, TPA may be useful to investigate the mol. mechanisms of suppressor circuit systems and the cytolytic mechanisms of NK and ADCC in various immune responses.

L6 ANSWER 40 OF 40 CA COPYRIGHT 1996 ACS DUPLICATE 39
AN 92:191210 CA
TI Chlorozotocin, an anti-**tumor** agent lacking bone marrow toxicity at therapeutic doses: effects on lymphocyte subpopulations in mice
SO Clin. Exp. Immunol. (1980), 39(2), 416-25
CODEN: CEXIAL; ISSN: 0009-9104
AU Fisher, R. I.; Mandell, G. L.; Bostick, Frieda; McMenamin, Mary G.; Anderson, T.
PY 1980
AB CDF1 mice which were injected i.p. with the LD10 of chlorozotocin (I) [54749-90-5] (20 mg/kg) developed a 50% redn. in circulating **peripheral blood lymphocytes** without a decrease in circulating granulocytes by day 3. Spleen wt. also decreased markedly. The percentage of spleen B and T cells, detd. by immunofluorescence with goat anti-mouse IgG and rabbit anti-mouse brain antisera, did not differ in control and I-treated mice. However, the ability of residual spleen cells to **proliferate** in response to phytohemagglutinin, concanavalin A, pokeweed mitogen, and allogeneic cells was significantly suppressed, although the lipopolysaccharide response was not reduced. The ability of the mice to respond to a primary immunization with sheep red blood cells was not significantly impaired. Therefore, I has a cytotoxic effect on both B and T cells but selectively inhibits the **proliferative** capacity of T cells. **B cell proliferation** and **B cell** function as measured in a primary **antibody** response were not reduced. Thus, I may be useful as an immunosuppressive drug as well as an **antitumor** agent.

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l52; d que l53
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L7          247 SEA FILE=BIOSIS ((PERIPHER? BLOOD OR PB)(W)LYMPHOCYT? OR
                PBL#) AND (B(W)(CELL# OR LYMPH?))
L8           61 SEA FILE=BIOSIS L7 AND (CANCER? OR CARCIN? OR NEOPLAS? OR
                 TUM? OR ANTICANCER? OR ANTICARCIN? OR ANTINEOPLAS? OR AN
                TITUM?)
L30          23 SEA FILE=BIOSIS L8 AND ANTIBOD?


L7          247 SEA FILE=BIOSIS ((PERIPHER? BLOOD OR PB)(W)LYMPHOCYT? OR
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L8           61 SEA FILE=BIOSIS L7 AND (CANCER? OR CARCIN? OR NEOPLAS? OR
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L15        3970 SEA FILE=MEDLINE (ANTIBODIES, MONOCLONAL+NT AND B-LYMPHOC
                YTES+NT)/CT
L16        3970 SEA FILE=MEDLINE L15 AND (LYMPHOCYTES+NT)/CT
L17         176 SEA FILE=MEDLINE L16 AND (D22.204.)/CT
L18          71 SEA FILE=MEDLINE L17 AND (ACTIVAT? OR PROLIF?)
L19           9 SEA FILE=MEDLINE L18 AND (BIND? OR BOUND?)
L31         248 SEA FILE=MEDLINE L8 AND ANTIBOD?
L32         103 SEA FILE=MEDLINE L31 AND (ACTIVAT? OR PROLIF?)
L33          14 SEA FILE=MEDLINE L32 AND (BIND? OR BOUND?)
L34          23 SEA FILE=MEDLINE L33 OR L19


L7          247 SEA FILE=BIOSIS ((PERIPHER? BLOOD OR PB)(W)LYMPHOCYT? OR
                PBL#) AND (B(W)(CELL# OR LYMPH?))
L8           61 SEA FILE=BIOSIS L7 AND (CANCER? OR CARCIN? OR NEOPLAS? OR
                 TUM? OR ANTICANCER? OR ANTICARCIN? OR ANTINEOPLAS? OR AN
                TITUM?)
L35          26 SEA FILE=BIOTECHDS L8 AND ANTIBOD?
L36          12 SEA FILE=BIOTECHDS L35 AND (ACTIV? OR PROLIF? OR BIND? OR
                 BOUND?)


L7          247 SEA FILE=BIOSIS ((PERIPHER? BLOOD OR PB)(W)LYMPHOCYT? OR
                PBL#) AND (B(W)(CELL# OR LYMPH?))
L8           61 SEA FILE=BIOSIS L7 AND (CANCER? OR CARCIN? OR NEOPLAS? OR
                 TUM? OR ANTICANCER? OR ANTICARCIN? OR ANTINEOPLAS? OR AN
                TITUM?)
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antineoplastic agent

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L37          251 SEA FILE=EMBASE L8 AND ANTIBOD?
L39          143 SEA FILE=EMBASE L37 AND (ACTIV? OR PROLIF?)
L40           23 SEA FILE=EMBASE L39 AND (BIND? OR BOUND?)


L7           247 SEA FILE=BIOSIS ((PERIPHER? BLOOD OR PB)(W)LYMPHOCYT? OR
                 PBL#) AND (B(W)(CELL# OR LYMPH?))
L8            61 SEA FILE=BIOSIS L7 AND (CANCER? OR CARCIN? OR NEOPLAS? OR
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                 TITUM?)
L41           34 SEA FILE=LIFESCI L8 AND ANTIBOD?
L43            5 SEA FILE=LIFESCI L41 AND (BIND? OR BOUND?)


L7           247 SEA FILE=BIOSIS ((PERIPHER? BLOOD OR PB)(W)LYMPHOCYT? OR
                 PBL#) AND (B(W)(CELL# OR LYMPH?))
L8            61 SEA FILE=BIOSIS L7 AND (CANCER? OR CARCIN? OR NEOPLAS? OR
                  TUM? OR ANTICANCER? OR ANTICARCIN? OR ANTINEOPLAS? OR AN
                 TITUM?)
L44          301 SEA FILE=CANCERLIT L8 AND ANTIBOD?
L45          126 SEA FILE=CANCERLIT L44 AND (ACTIVAT? OR PROLIF?)
L46           21 SEA FILE=CANCERLIT L45 AND (BIND? OR BOUND?)
L47         5616 SEA FILE=CANCERLIT (ANTIBODIES+NT AND B-LYMPHOCYTES+NT)/C
                 T
L48         5616 SEA FILE=CANCERLIT L47 AND (LYMPHOCYTES+NT)/CT
L49          425 SEA FILE=CANCERLIT L48 AND (D22.204.)/CT
L50          216 SEA FILE=CANCERLIT L49 AND (ACTIVAT? OR PROLIF?)
L51           27 SEA FILE=CANCERLIT L50 AND (BIND? OR BOUND?)
L52           48 SEA FILE=CANCERLIT L46 OR L51


L7           247 SEA FILE=BIOSIS ((PERIPHER? BLOOD OR PB)(W)LYMPHOCYT? OR
                 PBL#) AND (B(W)(CELL# OR LYMPH?))
L8            61 SEA FILE=BIOSIS L7 AND (CANCER? OR CARCIN? OR NEOPLAS? OR
                  TUM? OR ANTICANCER? OR ANTICARCIN? OR ANTINEOPLAS? OR AN
                 TITUM?)
L53            6 SEA FILE=WPIDS L8 AND ANTIBOD?

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                 PBL#) AND (B(W)(CELL# OR LYMPH?))
L8            61 SEA FILE=BIOSIS L7 AND (CANCER? OR CARCIN? OR NEOPLAS? OR
                  TUM? OR ANTICANCER? OR ANTICARCIN? OR ANTINEOPLAS? OR AN
                 TITUM?)
L41           34 SEA FILE=LIFESCI L8 AND ANTIBOD?
L42            8 SEA FILE=LIFESCI L41 AND (ACTIVAT? OR PROLIF?)


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L54          109 DUP REM L30 L34 L36 L40 L42 L43 L52 L53 (39 DUPLICATES
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=> fil biosi; s l30 and (activat? or prolif? or bind? or bound?)
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        323488 ACTIVAT?
        123581 PROLIF?
        364362 BIND?
        133666 BOUND?
L55          12 L30 AND (ACTIVAT? OR PROLIF? OR BIND? OR BOUND?)

=> dup rem l55,l34,l36,l40,l42,l43,l52,l53
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L56 98 DUP REM L55 L34 L36 L40 L42 L43 L52 L53 (39 DUPLICATES REMOVED)

=> d 1-98 bib abs; fil ca; e kuhajda f/au 10

L56 ANSWER 1 OF 98 BIOTECHDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 95-12601 BIOTECHDS
TI New immunostimulatory monoclonal **antibody**; against **B-lymphoblastoid** cells, produced by hybridoma cell culture
AU Hardy B; Novogrodsky A
PA MOR-Res.Appl.; Davis J T
PI WO 9520605 3 Aug 1995
AI WO 95-US1137 30 Jan 1995
PRAI IL 94-108501 31 Jan 1994
DT Patent
LA English
OS WPI: 95-275414 [36]
AN 95-12601 BIOTECHDS
AB A new immunostimulant monoclonal **antibody** (MAb) or antigen **binding** fragment **binds** to **B-lymphoblastoid** cells and induces **proliferation** and **activation** of **peripheral blood lymphocytes**, and has an **antitumor** effect. The MAb is produced by immunization of an animal with **B-lymphoblastoid** cells, lysed cells or a membrane preparation, followed by withdrawal of **B-lymphocytes**, immortalization, and selection of specific MAb-secreting cells. The MAb is produced by hybridoma CNCM I-1397. The MAb specifically **binds** to a protein of mol.wt. 48,000-50,000 (on gel electrophoresis). The MAb induces cytotoxic **activity** of lymphocytes, and may be used in therapy or prevention of **cancer**. It may also be used in therapy of other diseases, where **activation** or other immunomodulatory effects are therapeutic, e.g. early stages of HIV

infection, autoimmune disease and genetic or acquired immunodeficiency. (51pp)

L56 ANSWER 2 OF 98 BIOTECHDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 95-08691 BIOTECHDS
TI Non-human chimeric mammals;
obtained by engraftment of human peripheral blood leukocytes into an immuno-compromised mammal
AU Gallinger S; Hozumi N
PA Mount-Sinai-Hosp.
PI CA 2103693 7 Feb 1995
AI CA 93-2103693 6 Aug 1993
PRAI CA 93-2103693 6 Aug 1993
DT Patent
LA English
OS WPI: 95-131652 [18]
AN 95-08691 BIOTECHDS
AB A new method for non-human chimeric mammal production involves engraftment of human peripheral blood leukocytes (**PBLs**) into a non-human immunocompromised mammal and having 70% reconstitution of functional human leukocytes in the spleen. Also claimed are: a method for preparing a non-human chimeric mammal involving isolating human **PBLs**, obtaining an immunocompromised mammal depleted of functional T- and **B-lymphocytes**, treating the mammal with irradiation and with an **antibody** specific for the mammal's natural killer cells to deplete the mammal's natural killer cells, transplanting the human **PBLs** to the treated mammal, and maintaining the mammal; tissues, cells and cell products isolated from the chimeric animal; and a method for preparing **antibodies** to an antigen capable of eliciting an immune response in a human comprising immunizing a chimeric mammal with the antigen and isolating human **antibodies** which **bind** to the antigen from the mammal. The chimeric mammals can be used to study the immune response and graft versus host disease, for **antibody** production for use in diagnosis and therapy, and for disease and **tumor** drug testing. (80pp)

L56 ANSWER 3 OF 98 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 95-131652 [18] WPIDS
DNN N95-103523 DNC C95-060785
TI Non-human chimeric mammals - obtd. by engraftment of human peripheral blood leukocytes into an immuno-compromised mammal.
DC B04 D16 P14 S03
IN GALLINGER, S; HOZUMI, N; RODER, J C; SANDHU, J S; SHPITZ, B
PA (MOUN) MOUNT SINAI HOSPITAL CORP
CYC 1
PI CA 2103693 A 950207 (9518)* 80 pp
ADT CA 2103693 A CA 93-2103693 930806
PRAI CA 93-2103693 930806
AN 95-131652 [18] WPIDS
AB CA 2103693 A UPAB: 950518
The following are claimed: (A) a non-human chimeric mammal obtd. by

engraftment of human peripheral blood leukocytes (**PBLs**) into a non-human immunocompromised mammal and having 70% reconstitution of functional human leukocytes in the spleen; (B) a method of prepg. a non-human chimeric mammal comprising: (a) isolating **PBLs** from a human donor; (b) obtaining an immunocompromised mammal depleted of functional T and **B lymphocytes**; (c) treating the immunocompromised mammal with irradiation and with an **antibody** directed to the mammal's natural killer (NK) cells to deplete the mammal's NK cells; (d) transplanting the human **PBLs** into the treated mammal; and (e) maintaining the immunocompromised mammal having 70% reconstitution of functional human leukocytes in the spleen; (C) tissues, cells and cellular prods. isolated from a chimeric mammal as in (A); and (D) a method of prepg. **antibodies** to an antigen capable of eliciting an immune response in a human comprising immunising a chimeric mammal as in (A) with the antigen and isolating human **antibodies** which bind to the antigen from the chimeric mammal.

USE - The chimeric mammals can be used to assay substances that affect the human immune response esp. graft versus host disease. In addn., the mammals can be used to assay for substances that affect the human immune response to infectious agents and human **tumours**. Furthermore, the mammals can be used to assay for substances that modulate human allogenic graft rejection (all claimed). They can also be used for the prodn. of **antibodies** for use in diagnosis and therapy and for the prodn. of other human cell prods., e.g. lymphokines.

ADVANTAGE - The prepn. method results in rapid homing and consistent engraftment of high levels of human **PBLs** in the host spleen. A prim. and sec. immune response is consistently demonstrated shortly after engraftment against a number of defined antigens inoculated in vivo (claimed). The chimeric mammals show functional human NK cells, T cells, **B cells** and macrophages (claimed).

Dwg.0/12

L56 ANSWER 4 OF 98 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 2
AN 95:485099 BIOSIS
DN 98499399
TI Perinuclear anti-neutrophil cytoplasmic **antibodies** are spontaneously produced by mucosal **B cells** of ulcerative colitis patients.
AU Targan S R; Landers C J; Cobb L; MacDermott R P; Vidrich A
CS Cedars-Sinai IBD Cent., Suite D4063, Cedars-Sinai Med. Cent., 8700 Beverly Boulevard, Los Angeles, CA 90048, USA
SO Journal of Immunology 155 (6). 1995. 3262-3267. ISSN: 0022-1767
LA English
AB Approximately 60% of sera from ulcerative colitis (UC) patients contains Igs reactive with neutrophil components, raising the question of the origin of these anti-neutrophil cytoplasmic Abs (ANCA). Our assertion that ANCA is a marker for a mucosal disease-related immune response predicts the existence of ANCA producing **B cell** clones in the lamina propria

lymphocyte (LPL) fraction of UC patients. This hypothesis was tested by examining 1 2-day culture supernatants of LPL ANCA expression. LPL were isolated from surgically removed mucosa from patients with UC, Crohn's disease (CD), and diverticulitis. Normal mucosa was obtained from accident victims or normal margins of colon **cancer** resections. Supernatants were assayed by a fixed neutrophil ELISA. The ANCA staining pattern of supernatants expressing ANCA, as determined by ELISA, was assessed by indirect immunofluorescent staining of alcohol-fixed neutrophils. ANCA was found in 70% of culture supernatants from UC LPL fractions. In contrast, only approximately 11% of supernatants from CD and diverticulitis/normal (noninflammatory bowel disease (IBD)) LPL displayed ANCA **binding**. A perinuclear (pANCA) staining pattern was obtained with 70% of ANCA-expressing UC LPL supernatants, whereas ANCA-expressing CD and non-IBD LPL supernatants displayed a cytoplasmic reaction. **PBL** and mesenteric lymph node lymphocytes lacked spontaneous pANCA production, and pANCA production from **PBL** was not inducible. These findings indicate the existence of pANCA-producing **B cell** clones in mucosal lesions of UC patients and support our hypothesis that pANCA production is a consequence of a mucosal immune response specific to UC.

L56 ANSWER 5 OF 98 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 3
AN 95:248655 BIOSIS
DN 98262955
TI Expression of HOXC4 homeoprotein in the nucleus of **activated** human lymphocytes.
AU Meazza R; Faiella A; Corsetti M T; Airoldi I; Ferrini S; Bonicinelli E; Corte G
CS Advanced Biotechnol Center, CBA, V.le Benedetto XV 10, 16132 Genova, Italy
SO Blood 85 (8). 1995. 2084-2090. ISSN: 0006-4971
LA English
AB We have analyzed the expression of homeoproteins of the HOX family in resting and **activated** lymphoid cells and in **neoplastic** lymphoid cell lines by the use of monoclonal **antibodies** (MoAbs) already shown to react with the homeoproteins HOXA10, HOXC6, and HOXD4, respectively. AntiHOXA10 and C6 MoAbs DIDi not show any reactivity with the lymphoid cells tested, whereas anti-HOXD4 MoAb stained few resting **peripheral blood lymphocytes** (**PBLs**) and most phytohemagglutinin (PHA)-stimulated **PBLs** as early as 6 hours after stimulation. The pattern of staining of PHA-**activated PBLs** is reminiscent of the stages of nucleolar fragmentation in different phases of the cell cycle. The MoAb reacted also with **activated** or Epstein-Barr virus-transformed **B cells**, with clonal or polyclonal T and natural killer (NK) cells, with leukemic T-cell lines, and with a Burkitt's lymphoma cell line. RNAse protection experiments, per formed with probes specific for HOXD4 or for the highly homologous HOXD4, HOXB4, and HOXC4, belonging to the same paralogy group, indicated that only HOXC4 mRNA is present in resting

or **activated PBLs**. Northern blot analysis on polyA+ RNA from **activated PBLs** or Raji cells showed the presence of two different HOXC4 transcripts of 2.8 and 1.9 kb. Gel retardation and Southwestern blot assays showed the presence of a 32-kD homeoprotein with DNAbinding properties typical of a HOX4 homeoprotein in nucleolar extracts of PHA-**activated**, but not of resting, lymphocytes. Taken together, these data indicate that the HOXC4 homeoprotein is expressed in **activated** and/or **proliferating** lymphocytes of the T-, B-, or NK-cell lineage, whereas it is weakly expressed in a minority of resting cells, The early expression and the nucleolar localization suggest an involvement of HOXC4 in the regulation of genes controlling lymphocyte **activation** and/or **proliferation**.

L56 ANSWER 6 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 95352867 EMBASE
TI [The human **B-cell** repertoire: Expression in normal and pathological conditions].
LE REPERTOIRE B HUMAIN: EXPRESSION NORMALE ET PATHOLOGIQUE.
AU Huck S.; Zouali M.
CS Lab. d'immunogenetique moleculaire, UMR9942, IGMM, 1919 route de Mende, 34033 Montpellier Cedex 01, France
SO Medecine/Sciences, (1995) 11/11 (1566-1575).
ISSN: 0767-0974 CODEN: MSMSE4
CY France
DT Journal
FS 022 Human Genetics
026 Immunology, Serology and Transplantation
LA French
SL French; English
AB The timing and mechanisms that govern **B-cell** development are unique in several respects. Immunoglobulin (Ig) genes are exquisitely assembled in **B cells** and this process is site-specific. In order to express Ig on their surface, **B-cell** progenitors must rearrange variable (V) gene segments on the Ig heavy (H), and .kappa. and .lambda. light (L) chain loci in a process known as VDJ recombination. During human ontogeny, **B-cell** progenitors can choose from the libraries of variable gene segments. This primary repertoire is further expanded by junctional flexibility, secondary rearrangements, i.e. of VL to VL and somatic hypermutation. In human, the organization and the content of the Ig loci have been the focus of considerable attention. The recent elucidation of the structure of the VH and V.kappa. loci revealed that human Ig V genes exhibit unique features. For both loci, the V genes have been categorized into families of sequence-related members which are intermingled among each other and include approximately 45% of pseudo-genes. Even more intriguing are the observations that some VH and V.kappa. genes are dispersed not only outside the functional loci, but also on other chromosomes. The molecular events that gave rise to these 'orphon' genes underlie the extensive degree of plasticity of human Ig genes. While in normal conditions, they could play a role in amplifying the repertoire, in

pathological conditions they may in turn become the targets for chromosomal translocations in **B-cell neoplasia**. Other remarkable features of the human VH locus include its dominance by members of the VH3 gene-family and its high degree of polymorphism, with insertion deletion/polymorphisms and allelisms, which may lead to a high number of haplotypes with different coding potentials. The possibility that certain polymorphisms are associated with disease susceptibility has not been fully addressed. The elucidation of the content of the human Ig V loci is providing insight into the mechanisms of V gene expression in pathological conditions. A number of studies focused on V gene usage in relation to systemic autoimmunity. In principle, random combinatorial assembly of Ig V gene elements may lead to generation of a proportion of **antibodies** with high-affinity to self. In normal conditions, the corresponding **B cells** will be clonally deleted, rendered silent, or switched to a different specificity, a mechanism that has been termed receptor editing. In systemic autoimmunity, however, anti-self high-affinity **antibodies** are overexpressed. Molecular cloning, nucleotide sequencing and comparative genomic PCR revealed that human pathogenic autoantibody V genes have incurred extensive somatic selection events. There is also evidence that the corresponding **B cells** underwent essentially primary L-chain rearrangements. This observation raises the possibility that, in systemic autoimmunity, a subset of **B cells** may be unable to revise their receptors and to extinguish their high-affinity for self. This blockade could be genetically determined or somatically acquired. Finally, infection with the human immunodeficiency virus (HIV) results in several **B cell** abnormalities. The first evidence that HIV antigens may alter repertoire expression came from the demonstration that the major envelope protein of HIV-1, gp120, **binds** to V(H)3+ **B cells** and to serum V(H)3+ Ig from normal individuals, and this interaction is independent of the L-chain isotype. The gp120 interaction with V(H)3 gene products also seems to be functional because gp120 selectively induces Ig secretion by V(H)3 **B cells**. These characteristics are reminiscent of the properties of **B-cell** superantigens which are able to trigger a large proportion of the **B-cell** repertoire. More recently, studies of **peripheral blood lymphocytes** from HIV seropositive subjects and AIDS patients show marked changes in V(H)3+ **B cells** during different clinical stages of HIV infection. It is possible that the sequential expansion and reduction of V(H)3 **B cells** are related to the superantigenic properties of gp120. Understanding the molecular basis of this **activity** and the cellular mechanisms responsible for the clonal fate of **B cells** during HIV infection are relevant to designing novel strategies for immunointervention.

L56 ANSWER 7 OF 98 CANCERLIT
AN 95362854 CANCERLIT

TI Interleukin 4 **activates** a signal transducer and **activator** of transcription (Stat) protein which interacts with an interferon-gamma **activation** site-like sequence upstream of the I epsilon exon in a human B cell line. Evidence for the involvement of Janus kinase 3 and interleukin-4 Stat.
AU Fenghao X; Saxon A; Nguyen A; Ke Z; Diaz-Sanchez D; Nel A
CS Hart and Louise Lyon Laboratory, Department of Medicine, UCLA School of Medicine, University of California 90024-1680, USA.
NC AI-15251 (NIAID)
AI-34567 (NIAID)
SO J Clin Invest, (1995). Vol. 96, No. 2, pp. 907-14.
Journal code: HS7. ISSN: 0021-9738.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; Cancer Journals; L; Priority Journals
LA English
OS MEDLINE 95362854
EM 9510
AB Germ line C transcripts can be induced by IL-4 in the human B cell line, BL-2. Utilizing a IFN-gamma **activation** site-like DNA sequence element located upstream of the I epsilon exon, we demonstrated by gel mobility shift assays that IL-4 induced a **binding** activity in the cytosol and nucleus of BL-2 cells. This factor was designated IL-4 NAF (IL-4-induced nuclear-**activating** factors) and was identified as a tyrosine phosphoprotein, which translocates from the cytosol to the nucleus upon IL-4 treatment. Because these are the characteristics of a signal transducer and **activator** of transcription (Stat) protein, we determined whether antibodies to Stat proteins will interfere with gel mobility shift and found that antibodies to IL-4 Stat, also known as Stat6, but not antibodies to other Stat proteins, interfere with the formation of the IL-4 NAF complex. Congruous with the involvement of a Stat protein, IL-4 induced robust Janus kinase 3 (JAK3) activity in BL-2 cells. Cotransfection of JAK3 with IL-4 Stat into COS-7 cells produced an intracellular activity which **bound** the same IFN-gamma **activation** site-like sequence and comigrated with IL-4 NAF in electrophoretic mobility shift assay. These results show that IL-4 NAF is IL-4 Stat, which is **activated** by JAK3 in response to IL-4 receptor engagement.

L56 ANSWER 8 OF 98 BIOSIS COPYRIGHT 1996 BIOSIS
AN 95:365160 BIOSIS
DN 98379460
TI Subset Analysis of **Tumor** Infiltrating Lymphocytes and **Peripheral Blood Lymphocytes** in Malignant Glioma Patients.
AU Matsuhisa T
CS Dep. Neurol. Surg., Okayama Univ. Med. Sch., 2-5-1 Shikata-cho, Okayama 700, Japan
SO Brain and Nerve (Tokyo) 47 (5). 1995. 466-473. ISSN: 0006-8969
LA Japanese
AB It has already been reported that T cell infiltration is observed in brain **tumor** tissue but that general cellular immunity is

suppressed in malignant brain **tumor** patients. In this report, the subsets of **tumor** infiltrating lymphocytes (TILs) and **peripheral blood lymphocytes** (**PBLs**) were analyzed in 8 patients with malignant glioma in order to investigate the relationship between the local and systemic immunological response in malignant brain **tumor** patients TIL subsets in surgical specimens were analyzed immunohistochemically using the ABC method and monoclonal **antibodies** of the Leu series (anti-Leu 2a, 3a+b, 4+5b, 7, 12 and M5), and identified more precisely by double immunofluorescence staining (DIFS) using paired fluorescein isothiocyanate (FITC)-Leu 3a+b and phycoerythrin (PE)-Leu 8 or FITC-Leu 2a and PE-Leu 15. **PBL** subsets were determined preoperatively by two-color analysis with a fluorescence-**activated** cell sorter (FACS) using fluorescence-labeled monoclonal **antibodies** (paired FITC-Leu 4 and PE-Leu 12, FITC-Leu 3a and PE-Leu 8, or FITC-Leu 2a and PE-Leu 15). Most TILs proved to be T lymphocytes containing Leu 3a-b+ (T helper/inducer) cells and Leu 2a+ (T suppressor/cytotoxic) cells in almost equal numbers, but there were too few TILs to kill the **tumor** cells. Detailed examination by DIFS revealed that 93% of the Leu 3a+ **b+ cells** were helper T cells (Leu 3a+b+ cntdot Leu 8- cells) and that 88% of the Leu 2a+ cells were cytotoxic T cells (Leu 2a+ cntdot Leu15- cells). Analysis of **PBLs** showed statistically significant decreases in T cells as a whole and in helper T cells (Leu 3a+ cntdot Leu 8- cells). Suppressor T cells (Leu 2a+ cntdot Leu15+ cells) increased significantly, but there were no statistical differences from the control group in the other subsets. These findings indicate that an immunological response is induced in malignant glioma tissue, but not powerful enough to kill the **tumor** cells, and that systemic immunosuppression is induced in malignant brain **tumor** patients. It has been reported that malignant gliomas secrete immunosuppressive factors (e.g., transforming growth factor-beta-2, prostaglandin E-2, and interleukin-10) and that these factors suppress lymphocyte infiltration into **tumor** tissue. Our findings appear to corroborate these findings and suggest that enhancement of the local immune response and improvement of general cellular immunity should be taken into consideration when planning the treatment of malignant glioma.

L56 ANSWER 9 OF 98 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 4
AN 95:395775 BIOSIS
DN 98410075
TI **Activation** of human lymphocytes by a monoclonal **antibody** to **B lymphoblastoid** cells; molecular mass and distribution of **binding** protein.
AU Hardy B; Galli M; Rivlin E; Goren L; Novogrodsky A
CS Felsenstein Med. Res. Cent., Beilinson Campus, Petah-Tikva 49100, Israel
SO Cancer Immunology Immunotherapy 40 (6). 1995. 376-382. ISSN: 0340-7004
LA English
AB A novel monoclonal **antibody** (BAT) to the **B-**

lymphoblastoid cell line **activates** murine lymphocytes and exhibits a striking **antitumor** activity in mice. In order to evaluate the potential use of this **antibody** against human **cancer**, we have investigated its immuno-stimulatory properties on human **peripheral blood lymphocytes** (**PBL**). Our findings demonstrate that BAT mAb induces **proliferation** and cytotoxicity in human **PBL** against natural-killer-cell-sensitive and natural-killer-cell-resistant **tumor** cell lines. Interleukin-2 at a low concentration synergizes with BAT mAb in eliciting these effects. BAT mAb **binds** to human peripheral T cells as revealed by a double-labeling technique using anti-CD3 and BAT mAb. The molecular mass of the antigen recognized by BAT mAb was 48-50 kDa under reducing and non-reducing conditions. This study provides a basis for future experiments to evaluate the use of BAT mAb in the immunotherapy of **cancer**.

L56 ANSWER 10 OF 98 BIOSIS COPYRIGHT 1996 BIOSIS
AN 95:316988 BIOSIS
DN 98331288
TI CD8+ T lymphocytes are recruited to **neoplastic** cervix.
AU Bell M C; Edwards R F; Partridge E E; Kuykendall K; Conner W; Gore H; Turbat-Herrara E; Crowley-Nowick P A
CS Dep. Obstet. Gynecol. Reproductive Sci., Magee Womens Res. Inst., 204 Craft Ave., Pittsburgh, PA 15213, USA
SO Journal of Clinical Immunology 15 (3). 1995. 130-136. ISSN: 0271-9142
LA English
AB To-1iicIV distinguish normal cervical lymphocyte populations from phenotypes recruited to the cervix in response to cervical **neoplasia**, lymphocytes were isolated from normal and **neoplastic** cervix. A portion of the cervical transformation zone was obtained from 19 patients with pathologically confirmed cervical intraepithelial **neoplasia** and from 20 patients with normal cervices undergoing hysterectomy for benign indications. Mononuclear cells were harvested from cervical tissue using a serial, multienzymatic digestion procedure and enriched by density gradient centrifugation. Isolated cell populations were stained with surface marker-specific monoclonal **antibodies** and analyzed by fluorescent **activated** cell sorter to determine the percentage of **B cells**, total T cells, CD4+ T cells, CD8+ T cells, and natural killer (NK) cells. The distribution of circulating **peripheral blood lymphocyte** phenotypes was similar for both patients with **neoplasia** and normal controls. A marked disparity in the proportions of NK cells and T cells was demonstrated among lymphocyte phenotypes infiltrating the cervix. The percentage of CD4+ T cells and NK cells was contrast, the proportion of CD8+ T cells was significantly increased in the dysplastic tissue ($P = 0.0001$). Analysis of immunocompetent cells in the circulation appears to have little correlation with immunocytes present in the dysplastic epithelium. The depression in the proportion of CD4+ T lymphocytes and NK cells at the cervical squamocolumnar junction reflects a local

recruitment of CD8+ T cells to the site of **neoplasia** in the cervix.

L56 ANSWER 11 OF 98 BIOSIS COPYRIGHT 1996 BIOSIS
AN 95:255300 BIOSIS
DN 98269600
TI Autologous human **B-cell** immune response to pulmonary adenocarcinomatous polymorphic epithelial mucin.
AU Xiang J; Moyana T; Maksymiuk A
CS Saskatoon Cancer Cent., Div. Oncology, Univ. Saskatchewan, 20 Campus Drive, Sakatoon, Saskatchewan, 20 Campus Drive, Sakatoon, Saskatchewan S7N 4H4, Canada
SO Journal of Clinical Immunology 15 (2). 1995. 74-79. ISSN: 0271-9142
LA English
AB In order to investigate whether a **B-cell** immune response to the polymorphic epithelial mucin (PEM) is present in adenocarcinomatous patients, **peripheral blood lymphocytes** from 20 patients with adenocarcinomas from various sites were fused with the mouse-human heteromyeloma cell line SHM-D33. One IgM(K) monoclonal **antibody** derived from **peripheral blood lymphocytes** of a patient with a lung adenocarcinoma was generated with **binding** reactivity for bovine submaxillary mucin (BSM). The latter is one of the PEMs, and it contains a large amount of the **tumor** -associated sialosyl-Tn epitope. The generated **antibody** was designated KMD-2. Immunohistological studies on various tissues showed that KMD-2 reacted with 6/6 colorectal adenocarcinomas and 4/6 pulmonary adenocarcinomas. The **antibody** also displayed a slight degree of cross-reactivity with a limited number of normal tissues, especially those that elaborate mucin. Our data show that an autologous **antibody** response in the form of IgM to the immunosuppressive PEM is present in some adenocarcinomatous patients. The data also suggest that the KMD-2 (IgM/K) **antibody** may be of clinical importance for diagnostic purposes of adenocarcinomatous disease.

L56 ANSWER 12 OF 98 BIOSIS COPYRIGHT 1996 BIOSIS
AN 95:78898 BIOSIS
DN 98093198
TI Human immune response to DNP-modified autologous cells after treatment with a DNP-conjugated melanoma vaccine.
AU Sato T; Maguire H C Jr; Mastrangelo M J; Berd D
CS Thomas Jefferson Univ., 1015 Walnut St., Suite 1024, Philadelphia, PA 19107, USA
SO Clinical Immunology and Immunopathology 74 (1). 1995. 35-43. ISSN: 0090-1229
LA English
AB Immunizing patients with metastatic melanoma by injection of autologous **tumor** cells modified by DNP induces inflammatory responses in metastatic masses, which is sometimes associated with **tumor** regression. To elucidate this phenomenon, we studied the immune response to DNP-modified cells in these patients. All developed DTH to DNP-modified autologous lymphocytes (mean +- SE:

13.3 +- 1.3 mm), but not to TNP-modified lymphocytes. Larger responses (21.9 +- 3.6 mm) were elicited by DNP-modified autologous melanoma cells. In 8/11 patients tested, **PBL** **proliferated** in vitro when stimulated by autologous DNP-modified lymphocytes, and in 5 patients the stimulation resulted in production of interferon-gamma. DNP-modified autologous melanoma cells elicited lymphocyte responses as well. **PBL** from 1 patient were expanded by culture in IL2 and repeated restimulation with DNP-modified **B lymphoblastoid** cells. This T cell line **proliferated** and produced interferon-gamma but not IL4, when stimulated by autologous DNP-modified lymphocytes or melanoma cells. Both CD4+ and CD8+ subpopulations responded as determined by panning experiments and by testing of phenotypically homogeneous cultures obtained by limiting dilution. Studies of a stable CD8+ subline of the expanded T cells indicated that the response to DNP-modified cells was MHC-restricted, since it was blocked by **antibody** to class I determinants. Moreover, these T cells were able to respond to allogeneic DNP-modified stimulators that were matched at one or both HLA-A loci, but not to stimulators that were HLA-A mismatched. Finally, the CD8+ subline killed DNP-modified autologous melanoma cells, but not an HLA-A mismatched allogeneic melanoma, in a 6-hr 51Cr-release assay. These results may have significant implications for understanding the pathogenesis of drug-induced autoimmunity and for the development of new approaches to **cancer** immunotherapy.

L56 ANSWER 13 OF 98 BIOSIS COPYRIGHT 1996 BIOSIS
AN 95:488005 BIOSIS
DN 98502305
TI Lymphocyte subset reconstitution after allogeneic bone marrow transplantation using radiation-free conditioning regimen for patients with chronic granulocytic leukemia.
AU Milosevits J; Denes R; Poros A; Remenyi P; Batai A; Barta A; Masszi T; Lengyel L; Jakab K; Foldi J; Petranyi G; Kelemen E; Paloczi K
CS Natl. Inst. Haematol., Blood Transfusion Immunol., Semmelweis Univ. Med. Sch. Budapest, Hungary
SO International Journal of Hematology 62 (1). 1995. 27-33. ISSN: 0925-5710
LA English
AB Conditioning regimens for BMT are important in deter-mining transplant outcome. A radiation-free protocol containing Mitobronitol (DBM), Cytarabine (Ara-C) and Cyclophosphamide (Cy) was used for conditioning of patients with chronic granulocytic leukemia (CGL). Using this conditioning treatment, fewer transplant related complications, including acute GVHD, VOD and severe infections, were observed. Acute GVHD did not develop, but chronic GVHD, accompanied with graft-versus leukemia, was present in half of the cases. To determine the clinical effect of the DBM/Ara-C/Cy conditioning, the recovery of **peripheral blood lymphocytes** was examined after allogeneic BMT for patients with CGL in comparison with TBI/Cy conditioning. The lymphocyte subsets of 11 DBM patients were followed and analyzed periodically (30-90 days, 4-12 months and gt 13 months) using ten monoclonal **antibodies** and flow

cytometry. Decreased percentage of total T cells as well as CD4+ and CD8+ subpopulations, significantly decreased T cell **activation** and increased proportion of TCR-gamma-delta+ cells were found to be characteristic in the early post-transplant period in the DBM group. Early recovery and consistently higher percentage of **B cells** were observed for the whole follow-up period of patients receiving DBM conditioning. A high proportion of NK cells was observed in all transplant recipients. These findings suggest that the characteristic pattern of recovering lymphocytes is associated with the lack of severe transplant-related clinical complications following DBM/Ara-C/Cy conditioning.

L56 ANSWER 14 OF 98 BIOTECHDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 95-03912 BIOTECHDS
TI Monoclonal **antibody** against human lung **cancer** cells and hybridoma which produces the **antibody**; human monoclonal **antibody** production by human **B-lymphocyte** immortalization with Epstein-Barr virus, for use as a diagnostic and **antitumor** agent
PA Idemitsu
PI JP 06339392 13 Dec 1994
AI JP 93-153048 31 May 1993
PRAI JP 93-153048 31 May 1993
DT Patent
LA Japanese
OS WPI: 95-063353 [09]
AN 95-03912 BIOTECHDS
AB A new monoclonal **antibody** (MAb) reacts with human lung **cancer** cells but not with normal human cells, and has a **binding** affinity more than 2-fold higher than that of TOS/H8 towards human A549 lung **cancer** cells. The MAb may be used for diagnosis and immunotherapy of lung **cancer**. In an example, 30 ml **peripheral blood lymphocytes** were isolated from colon **cancer** patients, and were immortalized with Epstein-Barr virus. 10 Strains were selected, producing an MAb reacting with various **cancer** cells. These strains were fused with heteromyeloma SHM-D33 (ATCC CAL 1668), and fused cells were screened by ELISA. Cells reacting with Sq-19 but not with W1-38 (fibroblasts, ATCC CCL 75) were selected and cloned twice, followed by selection by tissue slice staining using lung **cancer** cells, lung **cancer** tissue and normal cells (sputum). Hybridoma D5-2-2, producing MAb D-2, was obtained. (5pp)

L56 ANSWER 15 OF 98 BIOTECHDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 95-01500 BIOTECHDS
TI A monoclonal **antibody** against a human **B-lymphoblastoid** cell line induces **tumor** regression in mice; application as an **antitumor** agent
AU Hardy B; Yampolski I; Kovjazin R; Galli M; Novogrodsky A
CS Felstein-Med.Res.Cent.Petah-Tikva; Univ.Tel-Aviv
LO The Felstein Medical Research Center, Beilinson Campus, Petah Tikva

49100, Israel.
SO Cancer Res.; (1994) 54, 22, 5793-96
CODEN: CNREA8 ISSN: 0008-5472
DT Journal
LA English
AN 95-01500 BIOTECHDS
AB A monoclonal **antibody** (BAT) to Daudi **B-lymphoblastoid** cell line membranes was developed. BALB/c mice were immunized by membranes from Daudi cells. Membranes were emulsified with complete Freund's adjuvant and administered i.m. and i.p., and s.c. After 3 wk, the mice were boosted i.v. with the membrane preparation in saline. Spleen cells harvested after 3 days were fused with myeloma NS-O cells using PEG. The hybridomas were grown in selective media. BAT was selected by its ability to **bind** the Daudi cell line in a cell-**bound** ELISA, and by its ability to induce **proliferation** of human **peripheral blood lymphocyte** (**PBL**). Splenocytes of BALB/c or C57BL given i.v. injections of 10 ug/mouse of BAT exhibited increased **proliferation** and cytotoxic **activity**. A single i.v. administration of BAT 2 wk after B16 melanoma cell inoculation resulted in a prominent **antitumor** effect as displayed by the elimination of lung metastases and prolonged survival of the treated mice. BAT was also effective in the regression of **tumors** in mice bearing 3LL (Lewis lung **carcinoma**) and MCA-105 (fibrosarcoma). (19 ref)

L56 ANSWER 16 OF 98 MEDLINE DUPLICATE 5
AN 95036340 MEDLINE
TI Anti-CD38-blocked ricin: an immunotoxin for the treatment of multiple myeloma [see comments].
CM Comment in: Blood 1995 Apr 15;85(8):2282-4
AU Goldmacher V S; Bourret L A; Levine B A; Rasmussen R A; Pourshadi M; Lambert J M; Anderson K C
CS ImmunoGen, Inc, Cambridge, MA 02139.
NC CA50947 (NCI)
SO Blood, (1994 Nov 1) 84 (9) 3017-25.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9502
AB We report the development of a potent anti-CD38 immunotoxin capable of killing human myeloma and lymphoma cell lines. The immunotoxin is composed of an anti-CD38 **antibody** HB7 conjugated to a chemically modified ricin molecule wherein the **binding** sites of the B chain have been blocked by covalent attachment of affinity ligands (blocked ricin). Conjugation of blocked ricin to the HB7 **antibody** has minimal effect on the apparent affinity of the **antibody** and no effect on the ribosome-inactivating activity of the ricin A-chain moiety. Four to six logs of CD38+ **tumor** cell line kill was achieved at

concentrations of HB7-blocked ricin in the range of 0.1 to 3 nmol/L. Low level of toxicity for normal bone marrow (BM) granulocyte-macrophage colony-forming units (CFU-GM), burst-forming units-erythroid (BFU-E), colony-forming units-granulocyte/erythroid/monocyte/macrophage (CFU-GEMM) cells was observed. Greater than two logs of CD38+ multiple myeloma cells were depleted from a 10-fold excess of normal BM mononuclear cells (BMMCs) after an exposure to HB7-blocked ricin under conditions (0.3 nmol/L) that were not very toxic for the normal BM precursors. HB7-blocked ricin was tested for its ability to inhibit protein synthesis in fresh patients' multiple myeloma cells and in normal BMMCs isolated from two healthy volunteers; **tumor** cells from four of five patients were 100-fold to 500-fold more sensitive to the inhibitory effect of HB7-blocked ricin than the normal BM cells. HB7 **antibody** does not **activate** normal resting **peripheral blood lymphocytes**, and HB7-blocked ricin is not cytotoxic toward these cells at concentrations of up to 1 nmol/L. The potent killing of antigen-bearing **tumor** cells coupled with a lack of effects on peripheral blood T cells or on hematopoietic progenitor cells suggests that HB7-blocked ricin may have clinical utility for the in vivo or in vitro purging of human multiple myeloma cells.

L56 ANSWER 17 OF 98 CANCERLIT
AN 94325561 CANCERLIT
TI Differential effects of gangliosides on Ig production and **proliferation** by human B cells.
AU Kimata H; Yoshida A
CS Department of Pediatrics, Kyoto University Hospital, Japan.
SO Blood, (1994). Vol. 84, No. 4, pp. 1193-200.
Journal code: A8G. ISSN: 0006-4971.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; Cancer Journals; L; Priority Journals
LA English
OS MEDLINE 94325561
EM 9410
AB The effects of gangliosides on human B-cell responses were studied. Of various gangliosides tested, only GM2 and GM3 inhibited production of IgG subclasses and IgM, but not IgA subclasses, and thymidine uptake by human B cells stimulated with SAC plus interleukin-2 (IL-2). In contrast, GM1, GD1a, GD1b, GD3, GT1b, and GQ1b were without effects. GM2- and GM3-induced inhibition were specific, because each was blocked by a corresponding antibody. Of various cytokines tested, tumor necrosis factor-alpha (TNF-alpha) alone counteracted GM2- and GM3-induced inhibitions of Ig production and thymidine uptake, whereas other cytokines including IL-1 beta, IL-3, IL-5, IL-6, and interferon-gamma each failed to do so. Moreover, anti-TNF-alpha antibody, but not control IgG, blocked the counteraction of inhibition by TNF-alpha. GM2 and GM3 each inhibited Ig production, thymidine uptake, and TNF-alpha production by surface IgG1+ (slG1+), sIgG2+, sIgG3+, sIgG4+, and sIgM+ B cells without affecting IL-2 **binding** or TNF-alpha **binding** to B cells, but had no such inhibitory effects on sIgA1+ or sIgA2+ B

cells. These findings indicate that GM2 and GM3 inhibit Ig production and thymidine uptake by human sIgG1+, sIgG2+, sIgG3+, sIgG4+, and sIgM+ B cells by inhibiting endogenous TNF-alpha production.

L56 ANSWER 18 OF 98 MEDLINE DUPLICATE 6
AN 94177635 MEDLINE
TI Human renal cell **carcinoma** cells are sensitive to the cytotoxic effect of a chimeric protein composed of human interleukin-4 and Pseudomonas exotoxin.
AU Puri R K; Debinski W; Obiri N; Kreitman R; Pastan I
CS Laboratory of Molecular Tumor Biology, Food and Drug Administration, National Institutes of Health, Bethesda, Maryland 20892.
SO Cell Immunol, (1994 Apr 1) 154 (1) 369-79.
Journal code: CQ9. ISSN: 0008-8749.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9406
AB We have previously demonstrated that functional high-affinity interleukin-4 receptors (IL-4R) are expressed on human renal cell **carcinoma** (RCC) cells (N. I. Obiri et al., J. Clin. Invest. 91, 88, 1993). In the present study, we examined the cytotoxic effect (determined by inhibition of protein synthesis) of a chimeric protein composed of human IL-4 and Pseudomonas exotoxin (PE) on human RCC **tumor** samples obtained from patients undergoing nephrectomy. The chimeric gene encoding hIL4-PE4E was constructed by fusing a cDNA clone for human IL-4 to the 5' end of a mutated cDNA encoding a full-length PE molecule. This gene was expressed in Escherichia coli, and large quantities of this recombinant protein were isolated to more than 95% purity. This chimeric protein, hIL4-PE4E, was highly cytotoxic to all six RCC cell lines examined. The concentration of hIL4-PE4E at which 50% inhibition of protein synthesis was obtained ranged from < 1 ng/ml (12 pM) to 10 ng/ml (120 pM) in five of the six isolates of RCC and 40-70 ng/ml in one other. A mutant chimeric protein which can **bind** to IL-4R but lacks the ADP ribosylation activity of PE was not cytotoxic to the RCC cells. The cytotoxic effect of hIL4-PE4E was IL-4R mediated because a fourfold molar excess of IL-4 abrogated the cytotoxic effect of hIL4-PE4E. A neutralizing monoclonal **antibody** to IL-4 also abrogated the cytotoxic effect of hIL4-PE4E. hIL4-PE4E showed very little cytotoxic activity to a normal human umbilical vein endothelial cell line (ID50 = 1000 ng/ml) and a human fibroblast cell line (ID50 approximately 400 ng/ml). Nonactivated human **peripheral blood lymphocytes** (**PBL**) were also insensitive to hIL4-PE4E (ID50, approximately 500 ng/ml), whereas phytohemagglutinin-**activated** **PBL** were highly susceptible to the cytotoxic effect of hIL4-PE4E (ID50, approximately 4 ng/ml). These data indicate that hIL4-PE4E may be a useful agent for the treatment of human RCC without affecting normal and resting immune cells.

L56 ANSWER 19 OF 98 CANCERLIT
AN 94130946 CANCERLIT
TI The phosphoprotein phosphatase calcineurin controls calcium-dependent apoptosis in B cell lines.
AU Bonnefoy-Berard N; Genestier L; Flacher M; Revillard J P
CS Laboratoire d'Immunologie, INSERM U80 UCBL, Hopital E. Herriot, Lyon, France.
SO Eur J Immunol, (1994). Vol. 24, No. 2, pp. 325-9.
Journal code: EN5. ISSN: 0014-2980.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; Cancer Journals; L; Priority Journals
LA English
OS MEDLINE 94130946
EM 9404
AB Group I Burkitt's lymphoma cell lines and the B104 lymphoma cell line which expresses a phenotype of immature B cells undergo apoptosis after cross-linking of their surface immunoglobulin (Ig) receptors or after exposure to a calcium ionophore, while protein kinase C (PKC)-**activating** phorbol esters prevent such apoptosis. We show here that blockade of the phosphoprotein phosphatase calcineurin or phosphatase 2B by cyclosporin A (CsA) also protects these B cell lines against Ca(2+)-dependent apoptosis but not against apoptosis triggered by the PKC inhibitor chelerythrine or by serum deprivation. Okadaic acid, an inhibitor of phosphatases 1, 2A and 2C was ineffective. Among a series of human cytokines tested, only interferon-alpha and tumor necrosis factor-alpha were shown to protect against Ca(2+)-dependent apoptosis when used alone or in combination with CsA. In contrast to phorbol esters which block the progression into the S/G2 phases of the cell cycle, CsA partially restored the **proliferation** of cells exposed to the calcium ionophore. Altogether these data provide indirect evidence for the control of B cell apoptosis by the serine/threonine phosphorylation status of yet undefined key cellular substrates.

L56 ANSWER 20 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 94137941 EMBASE
TI Isolation of naturally processed peptides from a Toxoplasma gondii-infected human **B lymphoma** cell line that are recognized by cytotoxic T lymphocytes.
AU Aosai F.; Yang T.-H.; Ueda M.; Yano A.
CS Department of Medical Zoology, Nagasaki Univ. School of Medicine, 1-12-4 Sakamoto, Nagasaki 852, Japan
SO J. PARASITOL., (1994) 80/2 (260-266).
ISSN: 0022-3395 CODEN: JOPAA2
CY United States
DT Journal
FS 004 Microbiology
026 Immunology, Serology and Transplantation
LA English
SL English
AB Naturally processed peptides derived from Toxoplasma gondii (T. gondii) were acid extracted from T. gondii-infected cells and

detected by cytotoxic T lymphocytes (CTL) derived from **peripheral blood lymphocytes** of a patient with chronic toxoplasmosis. The CTL lines were obtained by weekly in vitro stimulation with a T. gondii-infected human **B cell** lymphoma line, ARH, which shares HLA-A2 and -Cw4 determinants with the patient. The lytic **activity** of these CTL lines against T. gondii-infected ARH and ARH pulsed with fraction 29 of a reversed-phase high-performance liquid chromatography (HPLC) extract from T. gondii-infected ARH was inhibited by an anti-HLA-A, B, C monoclonal **antibody** (mAb) and an anti-HLA-A2 mAb. Anti-HLA-DR mAb failed to block the lytic **activity**. Thus, the presentation of peptides by T. gondii-infected cells for CTL is mediated by HLA-A2 molecules. Interestingly, antigen presentation of ARH pulsed with naturally processed HPLC fraction 29 peptides was not inhibited by treatment with brefeldin A. The amino acid sequence of the HLA-A2-**bound** peptide in fraction 29 was in part consistent with the predictive algorithm of HLA-A2-**binding** peptide motifs.

L56 ANSWER 21 OF 98 CANCERLIT
AN 95077666 CANCERLIT
TI [Regulation of the production of IgE in man]. Regulation de la production des IgE chez l'homme.
AU Dessaint J P; Labalette M
CS Service d'Immunologie, Centre Hospitalier, Faculte de Medecine, Lille.
SO Allerg Immunol (Paris), (1994). Vol. 26, No. 7, pp. 238-47. Journal code: AEI. ISSN: 0397-9148.
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
FS MEDL; L; Priority Journals
LA French
OS MEDLINE 95077666
EM 9502
AB Allergy is associated with elevated production of allergen-specific IgE antibody. Naive allergen-specific B cells undergo a series of molecular interactions before they would produce allergen-specific IgE antibody. Besides allergen recognition, specific B cells have to receive signals from cell-surface proteins and cytokines from their various cellular partners. **Activated** T cells express a ligand for CD40 that rescues germinal centre B cells from programmed cell death. Contact with follicular dendritic cells or other T and B cells promotes differentiation into plasma through engagement of two pairs of complementary cell-surface proteins, CD21/CD23. Among the many cytokines secreted by helper T cells, interleukin-4 is necessary for the class switch to IgE, and IL-13 also triggers switching to IgE. Then, IgE would participate to feed-back regulation of its production by acting at different levels. When **bound** to CD23, also known as Fc epsilon receptor type II, IgE immune complexes inhibit CD21/CD23 cell-cell interactions. When **bound** to Fc epsilon receptor type I on Langerhans' cells in the skin or mucosa, IgE antibody enhances allergen presentation to T

cells and promotes their differentiation into type 2 helper T cells that secrete IL-4 but no interferon-gamma. Local **activation** of mast cells or basophils, via their Fc epsilon Receptor type I-**bound** IgE, would trigger secretion of various cytokines, IL-4 in particular, and expression of CD21 and CD40 ligand, which altogether could replace contact with T cells to deliver the co-stimulatory signals for localised IgE production.(ABSTRACT TRUNCATED AT 250 WORDS) (43 Refs)

L56 ANSWER 22 OF 98 CANCERLIT
AN 94314368 CANCERLIT
TI Two different IFN-gamma nonresponsive variants derived from the B-cell lymphoma 70Z/3.
AU Rhodes L D; Paull A T; Sibley C H
CS Department of Biological Structure, University of Washington, Seattle 98195.
NC P01 GM42508 (NIGMS)
NIGMS T32 GM 07270 (NIGMS)
SO Immunogenetics, (1994). Vol. 40, No. 3, pp. 199-209.
Journal code: GI4. ISSN: 0093-7711.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; Cancer Journals; L; Priority Journals
LA English
OS MEDLINE 94314368
EM 9409
AB The kappa immunoglobulin (Igk) light chain locus is transcriptionally silent in the mouse B-cell lymphoma 70Z/3. However, exposure to lipopolysaccharide (LPS) or interferon-gamma (IFN) causes a marked increase in Igk transcription. By immunoselection, we isolated two variants that are nonresponsive to IFN. One variant, AT7.2, has retained its response to LPS (IFN-LPS+), whereas the other, AT3.3, is also nonresponsive to LPS (IFN-LPS-). Stable transfection of an intact Igk gene does not rescue the phenotype of either variant. Both variants have intact Igk genes and neither is deficient in the **binding** or uptake of IFN. Nuclear extracts from LPS-treated wild-type 70Z/3 cells show strong increases in three transcription factors: OTF-2, NF-kappa B, and kBF-A. Remarkably, when the IFN-LPS- variant is treated with LPS, all three transcription factors are still observed in the nuclear extracts. Treatment of wild-type cells with either LPS or IFN also causes a decrease in nuclear complexes that **bind** to two other regions of the Igk intron enhancer, the octenh and the E kappa MHCIC regions. Both of these changes are also observed after LPS or IFN treatment of the IFN-LPS- variant. Thus, this variant transduces the IFN and LPS signals at least into the nuclear compartment, but still fails to **activate** Igk transcription. In contrast, the IFN-LPS+ variant decreases neither the octenh nor the E kappa MHCIC **binding** complexes in response to IFN. This variant may be defective in transducing the IFN signal to the nucleus. These variants will be useful in studying the **activation** of Igk transcription and the IFN signaling pathway in B cells.

L56 ANSWER 23 OF 98 BIOSIS COPYRIGHT 1996 BIOSIS
AN 94:360734 BIOSIS
DN 97373734
TI Low level CD20 expression on T cell malignancies.
AU Warzynski M J; Graham D M; Axtell R A; Zakem M H; Rotman R K
CS West Mich. Flow Cytometry Serv., Ferguson-Blodgett Hosp., 72 Sheldon Blvd. S.E., Grand Rapids, MI 49503, USA
SO Cytometry 18 (2). 1994. 88-92. ISSN: 0196-4763
LA English
AB Although initially thought to be a B lineage restricted antigen, low "density" or **antibody binding** capacity (ABC) CD20 has recently been detected on subset(s) of normal T lymphocytes (Hultin et al.: Cytometry 14:196-204, 1993). We report low ABC CD20 expression in three (two children, one adult) cases of T-acute lymphoblastic leukemia (T-ALL). CD20 and other pertinent antigens were detected using a direct dual color method with a Becton Dickinson FACScan flow cytometer and Simulset software. Only one cell population based on light scatter was noted in each case that immunophenotypically represented almost a pure population of malignant cells expressing T lymphocyte antigens (for example, CD7 98%, 92%, and 100%, respectively). A total of 95%, 87%, and 79% of the cells from the three cases expressed CD20 with an unusual low ABC compared to the customary "bright" CD20 expression on normal **B lymphocytes**. Other **B lymphocyte** associated antigens, such as CD19, CD22, Dr, and immunoglobulin light chains, were negative. Eleven other T lymphocytic malignancies from 1991 to 1993 were CD20 negative, including three other case of T-ALL (one adult and two children). One unusual case of intestinal small lymphocytic non-Hodgkin's lymphoma with a natural killer/T lymphocytic immunophenotype not described in this report appeared to be CD20"dim". Low ABC CD20 expression by T lymphocytic malignancies may provide a more unique immunophenotypic "fingerprint" to help support the diagnosis of T cell **neoplasia** vs. normal/reactive T cells (for example, low ABC CD20 cells represent only 2.4 +- 1.5% of normal **peripheral blood lymphocytes**). This characteristic might also facilitate monitoring patients for residual or recurrent disease. The prognostic significance of CD20 co-expression is uncertain and must await further studies.

L56 ANSWER 24 OF 98 MEDLINE DUPLICATE 7
AN 95162036 MEDLINE
TI EBV gene expression, EBNA **antibody** responses and EBV+ **peripheral blood lymphocytes** in post-transplant lymphoproliferative disease.
AU McKnight J L; Cen H; Riddler S A; Breinig M C; Williams P A; Ho M; Joseph P S
CS Department of Infectious Diseases and Microbiology, Graduate School of Public Health, University of Pittsburgh, Pennsylvania 15261.
NC 2 SO7 RR05451-26 (NCRR)
2 SO7 RR05451-27 (NCRR)
2 SO7 RR05451-28 (NCRR)
+

SO Leuk Lymphoma, (1994 Sep) 15 (1-2) 9-16. Ref: 51
Journal code: BNQ. ISSN: 1042-8194.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9505
AB Epstein-Barr virus (EBV) is associated with the development of several **B cell** malignancies including Burkitt's lymphoma (BL), post-transplant lymphoproliferative disease (PTLD), and AIDS-related lymphomas. The latter two diseases result from EBV-driven **B cell proliferation** in the absence of normal immunosurveillance and as such, represent a heterogenous family of lymphoproliferative disorders. This article reviews studies on EBV gene expression and **antibody** development in PTLD and introduces recent information on the levels of EBV+ **peripheral blood lymphocytes** to discuss possible mechanisms of pathogenesis under varying conditions of immunosuppression.

L56 ANSWER 25 OF 98 BIOSIS COPYRIGHT 1996 BIOSIS
AN 94:548135 BIOSIS
DN 98007683
TI Double immunocytochemical evaluation of lymphoid cell **proliferation** and line in different lymphoproliferative diseases.
AU Malashenko O S; Samoilova R S; Bulycheva T I
CS Hematol. Sci. Cent., Russ. Acad. Med. Sci., Moscow, Russia
SO Gematologiya i Transfuziologiya 39 (3). 1994. 3-7. ISSN: 0234-5730
LA Russian
AB The increased range of the diagnostic criteria and the introduction of the classification scheme "Practical Formulation of Non-Hodgkin's Lymphomas for Clinical Application" made the authors to study **proliferative** potential of lymphoid cells with identification of the cell line affiliation. The investigation was carried out with the use of the double immunocytochemical test employing anti-nuclear (Ki-67) and line-specific monoclonal **antibodies** on **peripheral blood lymphocytes**, those of lymph nodes and bone marrow obtained from 40 patients with lymphoproliferative diseases and on the cells of lymphoblastoid line 501. The disease variant was classified according to the WHO criteria. The highest (gt 60%) **proliferative** activity of lymphoid cells was found in the bone marrow in acute non-T non-**B lymphoblast** leukemia and in lymph node in T-cell and non-T non-**B-cell** lymphoblast lymphosarcoma. A broad range in the number of **proliferative** cells existed among **B-cell** lymphosarcomas of lymphoblast (12-73%) and prolymphocytic (0-91%) variants. Together with heterogeneous immunological phenotype, this reflects a wide spectrum of various nosological entities recognized by the WHO classification as lymphoblast and prolymphocytic variants of lymphosarcoma, says

about the defects of the above classification. Extremely low (lt 1%) percent of **proliferative**, cells was observed in **B -cell** chronic lymphoid leukemia and hairy-cell leukemia. These differences in **tumor** cell **proliferative** potential in different lymphoproliferative diseases agree with the views on maturation and differentiation of lymphoid calls. The data obtained by the authors support the necessity of corroding routine histological data by immunological characteristics of pathological lymphoid cells, primarily, by introduction of data on cell **proliferative** activity. According to the proposed classification scheme, the key criterion is the malignancy of **tumor** cell population determined by **proliferative** activity of the clone pathological cells.

L56 ANSWER 26 OF 98 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 8
AN 94:110269 BIOSIS
DN 97123269
TI A novel 120-kDa antigen shared by immature human thymocytes and long-term-**activated** T cells.
AU Fabbi M; Tiso M; Gangemi R M R; Favre A; Demartini P; Bargellesi-Severi A
CS Immunobiol., IST, Ist. Nazionale Ricerca sul Cancro, Viale Benedetto XV, 10, I-16132 Genova, ITL
SO European Journal of Immunology 24 (1). 1994. 1-7. ISSN: 0014-2980
LA English
AB In this study we report the characterization of monoclonal **antibody** (mAb) 8B4/20, raised against immature human thymocytes, that identifies a novel leukocyte antigen. The molecular characterization of the antigen by immunoprecipitation and immunoblotting yields, under nonreducing conditions, a specific band of 120 kDa which, under reducing conditions, displays a slightly lower molecular mass (110 kDa). mAb 8B4/20 detects a molecule found on the majority of thymocytes with an inverted gradient of expression when compared to CD3. It appears at high density on the CD3-/low thymocytes, at reduced density on the CD3-med and double-positive thymocytes, and is absent on CD3-hi and single-positive thymocytes and on peripheral blood T cells. Immunohistochemistry on frozen sections demonstrates cortical staining of the thymic lobules. Flow cytometric analysis of the different subsets of peripheral blood mononuclear cells shows that mAb 8B4/20 detects an antigen expressed only on CD56+/CD16+ natural killer cells and on a fraction of CD14+ monocytes. T cells, **B cells**, erythrocytes, granulocytes and platelets are consistently negative. The expression of the molecule on **tumor** cell lines does not show lineage restriction. Analysis of phytohemagglutinin plus recombinant interleukin-2-**activated peripheral blood lymphocytes** shows that mAb 8B4/20 identifies an antigen expressed on CD3+ cells by week 3 of culture. Thus, it recognizes a very late **activation** antigen (VLA) on mature T cells. The cell distribution and the electrophoretic pattern of the molecule identified by mAb 8B4/20 is distinct from that of known CD and of integrin-NLA molecules. Its function on thymocytes is so far unknown; however, the **binding** of mAb 8B4/20 to **tumor** lines

induces changes in the morphology and adhesive properties of the 8B4/20+ cells growing in suspension. We suggest that mAb 8B4/20 recognizes a molecule that may be involved in interactions between thymocytes and other thymic structures that may be relevant for the selection process.

L56 ANSWER 27 OF 98 LIFESCI COPYRIGHT 1996 CSA
AN 94:88657 LIFESCI
TI High level functional engraftment of severe combined immunodeficient mice with human **peripheral blood lymphocytes** following pretreatment with radiation and anti-asialo G sub(M1)
AU Shpitz, B.; Chambers, C.A.; Singhal, A.B.; Hozumi, N.; Fernandes, B.J.; Roifman, C.M.; Weiner, L.M.; Roder, J.C.; Gallinger, S.
CS Div. Mol. Immunol. and Neurobiol., Samuel Lunenfeld Res. Inst., Suite 1225, Mount Sinai Hosp, 600 University Ave., Toronto, ON M5G 1X5, Canada
SO J. IMMUNOL. METHODS, (1994) vol. 169, no. 1, pp. 1-15. ISSN: 0022-1759.
DT Journal
FS F; W3
LA English
SL English
AB The severe combined immunodeficient (SCID) mouse engrafted with human **peripheral blood lymphocytes** (**PBLs**) is a potentially useful model for the study of **cancer** immunotherapy. For this application, rapid, consistent, and high level engraftment of SCID mice with functional human cytotoxic effector cells is necessary. To date, short term human lymphoid cell engraftment in SCID mice has generally been low and variable. Further, most of the human cells detected within the first 30 days are found in the peritoneal cavity. The purpose of the present study was to improve short term reconstitution of human **PBLs** in the SCID mouse. Depletion of SCID mouse natural killer (NK) cells with anti-asialo G sub(M1) only marginally improved short term reconstitution with human CD3 super(+) cells. Human T cells positive for CD4, CD8, TcR alpha beta , and TcR gamma delta , and human NK and **B cells** were detected in the spleens of irradiated plus anti-asialo G sub(M1) pretreated SCID mice. The presence of human lymphoid cells was confirmed by immunohistologic staining. The human immune cells in these mice were shown to be functional by the in vivo demonstration of an appropriate secondary immune response to the injection of tetanus toxoid and by an in vivo **proliferative** response to phytohemagglutinin. Human NK cells could be found in the spleens and peripheral blood of irradiated plus anti-asialo G sub(M1) pretreated mice. These cells were also shown to be competent by their ability to lyse the human NK sensitive **tumor** targets K562 and MOLT-4 in super(51)Cr release assays. Thus, pretreatment of SCID mice with radiation plus anti-asialo G sub(M1) significantly improves short term human **PBL** engraftment and provides a potentially useful model for the study of **cancer** immunotherapy.

L56 ANSWER 28 OF 98 CANCERLIT
AN 94697526 CANCERLIT
TI Clinical experience with B-cell-specific antibodies and cytokines (Meeting abstract).
AU Rankin E M
CS The Netherlands Cancer Inst., Antoni van Leeuwenhoek Huis, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands
SO Non-serial, (1993). EACR-12: 12th Biennial Meeting of the European Association for Cancer Research. April 4-7, 1993, Brussels, Belgium, 1993.
DT (MEETING ABSTRACT)
FS ICDB
LA English
EM 9411
AB Malignancies of B-lymphoid origin are unrivalled for evaluating the effects of monoclonal therapy because they express a number of well characterized antigens, seem to be sensitive to immune manipulation, are more accessible than solid tumors and patients are less likely to make anti-antibodies. Successful treatment with unmodified antibodies depends on recruitment of host effector mechanisms, including antibody dependent cellular cytotoxicity (ADCC), complement-mediated cytotoxicity and the **activation** of natural killer cells (NK), monocytes and cytotoxic T lymphocytes (CTLs). We have shown that recombinant interleukin-2 (rIL-2) given by continuous infusion for 6 wk or more gives a sustained increase in NK cells and ADCC capacity (Vlasveld et al, Br J Cancer 65:744-50, 1992; Br J Cancer 1993, in press). Our initial clinical study with the murine IgG2a monoclonal antibody CLB-CD19 directed against the B-cell-specific CD19 antigen demonstrated the antitumor activity and safety of this antibody (Hekman et al, Cancer Immunol Immunother 32:364-72, 1991). To achieve a better antitumor effect, we combined 50 mg/m2 CLB-CD19 given twice weekly with continuous infusion of rIL-2 (3 x 10(6) IU/m2/24 hr) for a period of 12 wk on an outpatient basis. We tested this regimen in 7 patients (age 43-65 yr) in good clinical condition with heavily pretreated, slowly progressive low-grade non-Hodgkin's lymphoma. The dose of CLB-CD19 was adjusted to maintain a trough serum level greater than 1 ug/ml (measured 3 days after previous infusion). Treatment was well tolerated with minor side effects, such as flulike syndrome and fatigue. Toxicity coincided with the peak eosinophilia and peak serum soluble IL-2 receptors at 3 wk and resolved thereafter. There was evidence of T-cell **activation** during therapy. There was a gradual rise in CD8+dim CD56+bright cells with a corresponding increase in p75 expression. The number of CD3+ cells bearing CD25 increased, in 3 cases by greater than 50%. There were increases in NK and LAK cell activity and in ADCC in both peripheral blood and lymph node lymphocytes. We could find no evidence of CTLs directed against processed murine immunoglobulin (Ig). The number of circulating B cells fell during treatment particularly in those with circulating malignant lymphocytes. B cells in the blood were saturated with antibody after 1 wk of treatment. Penetration of antibody to lymph nodes was demonstrated in all pts, in most cases

saturation of lymph node **binding** sites was also achieved. There were no changes in T or NK cell infiltrates in the nodes during therapy. Modulation of antigen expression in blood or lymph node cells occurred in most patients but this did not abrogate the antitumor effect. No changes in serum Ig or complement levels were seen. No antibodies to rIL-2 or infused murine Ig were detectable. An antitumor effect was seen in 6 patients by week 4 but was not durable; only one patient had a persistent greater than 50% reduction in tumor vol lasting greater than 1 mo. While this study confirms the potential of immunotherapy using monoclonal antibodies and rIL-2, other strategies are needed to produce a durable effect. Our early experience with the CAMPATH-1H antibody (Wellcome Ltd) confirms the antitumor activity of this human antibody directed against the pan-lymphocyte antigen CDw52. All patients, however, experienced side effects with fever and rigors, which sometimes resolved with continuing treatment but which were not dose=related. There were no changes in serum complement levels though we did demonstrate **binding** of C3a to peripheral lymph node cells after CAMPATH-1H infusion. Development of an antitumor response showed some correlation with the cytokine profile in vivo (eg, IL-6 and IL-8). Presumably, the lysis of T cells in vivo is responsible for this secondary cytokine release. CAMPATH-1H seems promising but measures to ameliorate the side effects without altering the antitumor effect are needed.

L56 ANSWER 29 OF 98 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 93-320763 [40] WPIDS
DNC C93-142809
TI Prepn. of human monoclonal **antibodies** against self antigens - using secondary lymphoblasts from mixed lymphocyte response between memory **B lymphocytes**, lymphocytes and antigen.
DC B04 D16
IN WHITAKER, R B; WHITAKER, R
PA (IMMU-N) IMMUNET
CYC 20
PI WO 9319197 A1 930930 (9340)* EN 53 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9339232 A 931021 (9407)
EP 651819 A1 950510 (9523) EN
R: CH DE FR GB IT LI
JP 07507923 W 950907 (9544) 11 pp
ADT WO 9319197 A1 WO 93-US2479 930318; AU 9339232 A AU 93-39232 930318; EP 651819 A1 EP 93-908394 930318, WO 93-US2479 930318; JP 07507923 W JP 93-516719 930318, WO 93-US2479 930318
FDT AU 9339232 A Based on WO 9319197; EP 651819 A1 Based on WO 9319197; JP 07507923 W Based on WO 9319197
PRAI US 92-856088 920320
AN 93-320763 [40] WPIDS
AB WO 9319197 A UPAB: 931129
Prepn. of human monoclonal **antibody** (MAb) against an antigen comprises forming a mixt. of (i) a prepn. of human

lymphocytes enriched from memory **B lymphocytes** and obtd. from a donor seropositive for the antigen, (ii) a prepn. of lymphocytes from a second donor that is allogeneic w.r.t. the first donor, and (iii) the antigen to generate a mixed lymphocyte response, and the prodn. of secondary lymphoblast progency of the memory **B lymphocytes**. Some of this progeny are then fused with heterohybrid fusing partners, and a fused cellular prod. isolated with binding specificity for the antigen.

The MAb has binding specificity for human IgA or IgC, or human CD antigens. The prepn. of lymphocytes from the second donor includes splenocytes.

USE/ADVANTAGE - The MAb has high affinity for the antigen. The MAbs are pref. specific for human self antigens, such as immunoglobulin, antigens involves in autoimmune disease and **cancer** antigens. They may also be directed against bacterial, vviral parasitic and other infectious agent antigens. The memory **B lymphocytes** may be obtd. fro a non-human mammal with a human immune system this permits the prepn. of MAbs by immunising the non-human mammal, so avodiing ethnical and medical considerations. This mammal is pref. a SCID mouse. An advantage of using the mixed lymphocyte response is that time consuming and complex methods of prior art procedures for providing growth factors for **peripheral blood lymphocytes** to stimulate lymphoblast formulations are avoided.

Dwg.0/3

L56 ANSWER 30 OF 98 LIFESCI COPYRIGHT 1996 CSA
AN 94:22699 LIFESCI
TI A majority of Ig H chain cDNA of normal human adult blood lymphocytes resembles cDNA for fetal Ig and natural autoantibodies
AU Huang, C.; Stollar, B.D.*
CS Dep. Biochem., Tufts Univ. Sch. Med., 136 Harrison Ave., Boston, MA 02111, USA
SO J. IMMUNOL., (1993) vol. 151, no. 10, pp. 5290-5300. ISSN: 0022-1767.
DT Journal
FS F
LA English
SL English
AB Certain Ig V sub(H) gene segments, with few or no mutations, recur frequently in natural autoantibodies, fetal **antibodies**, and products of **B cell tumors**. The goal of this study was to determine whether similar Ig gene segment usage occurs in normal human adult **PBL**. Extending previous analyses, 105 randomly picked H chain V region clones of representative cDNA libraries from **PBL** were sequenced. Clones were from: IgM and IgG libraries from one RNA sample of a normal adult; a second IgM library from the same subject 11 mo later; and one IgM library from a second subject. The circulating **B cell** population may represent a distinct compartment, with a large proportion of cells similar to those of the fetal and natural autoantibody repertoire. Polyreactive Ig

products of these circulating cells may serve a screening function, **binding** and delivering diverse Ag to secondary lymphoid tissues where more highly selective **antibodies** are formed to foreign or self-Ag.

L56 ANSWER 31 OF 98 LIFESCI COPYRIGHT 1996 CSA
AN 94:11056 LIFESCI
TI Lymphoproliferation in primary Sjoegren's syndrome. Evidence of selective expansion of a **B cell** subset characterized by the expression of cross-reactive idiotypes
AU Shokri, F.; Mageed, R.A.; Maziak, B.R.; Talal, N.; Amos, N.; Williams, B.D.; Jefferis, R.
CS Dep. Immunol., Sch. Public Health, Univ. Med. Sci. Tehran, Tehran, P.O. Box 6446-14155, Iran
SO ARTHRITIS RHEUM., (1993) vol. 36, no. 8, pp. 1128-1136. ISSN: 0004-3591.
DT Journal
FS F
LA English
SL English
AB The objective was to evaluate the possibility that lymphoproliferation in primary Sjoegren's syndrome (SS) arises within a subset of **B cells**. A panel of monoclonal **antibodies** (MAb) specific for rheumatoid factor (RF)-associated cross-reactive idiotypes (CRI) and anti-V Kappa and anti-V sub(H) subgroup **antibodies** were used to define the clonality of **B lymphocytes** undergoing **neoplastic** transformation in 5 patients with primary SS. Anti-CRI **antibodies** were also used to study longitudinal variations in serum paraprotein levels and in vitro regulation of IgM and IgM-RF production by **peripheral blood lymphocytes**. The levels of CRI, IgM, and IgM-RF were quantitated in serum and culture supernatants by enzyme-linked immunosorbent assay. heavy and light chain isotypes and V sub(H) subgroups of the paraproteins were determined by immunoelectrophoresis, immunofixation, and Western blotting. The results suggest that lymphoproliferation in primary SS is highly selective, and that the anti-CRI **antibodies** can be used as an aid to early diagnosis as well as for monitoring and modulating the lymphoproliferative process in primary SS.

L56 ANSWER 32 OF 98 MEDLINE DUPLICATE 9
AN 93315232 MEDLINE
TI Identification of colon-**tumor**-associated antigens by T-cell lines derived from **tumor**-infiltrating lymphocytes and **peripheral-blood lymphocytes** from patients immunized with an autologous **tumor**-cell/bacillus Calmette-Guerin vaccine.
AU Ransom J H; Pelle B A; Hubers H; Keynton L M; Hanna M G Jr; Pomato N
CS Organon Teknika/Biotechnology Research Institute, Rockville, MD 20850.
SO Int J Cancer, (1993 Jul 9) 54 (5) 734-40. Journal code: GQU. ISSN: 0020-7136.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9310
AB **Tumor** immunity developing as a response to an autologous colon-**tumor**/bacillus Calmette-Guerin (BCG) vaccine appears to be associated with induction of CD4+ helper T cells, implied by the observation that vaccine efficacy is associated with major histocompatibility complex class-II molecule expression on the vaccine **tumor** cells. Therefore, in an attempt to identify colon-**tumor**-associated antigens responsible for conferring immunity, we examined and compared the **proliferative** responses of **peripheral-blood lymphocytes** (**PBL**) from patients immunized with the autologous **tumor**/BCG vaccine to T-cell lines cloned expanded from colon-**tumor**-infiltrating lymphocytes to 5 antigens isolated on the basis of their reactivity by colon-**tumor**-reactive human monoclonal **antibodies**. Enzymatically dissociated colon **tumors** provided a source for establishment of cloned T-cell lines, **tumor** cell lines propagated in vitro or in vivo as nude-mouse xenografts and EBV-transformed **B-cell** lines used as antigen-presenting cells. Of 104 different T-cell lines tested, only 3 **proliferated** in response to CTAA 28A32-46K, and I to the CTAA28A32-32K antigen. In contrast, **PBL** from 64% of patients immunized with the autologous colon-**tumor**/BCG vaccine responded to the CTAA 28A32-32K antigen. This antigen is related to a family of calcium- and phospholipid-**binding** placental proteins termed annexins. Since **proliferative** responses developed to this antigen after vaccination in 64% of individuals, this antigen may be an important common colon-**tumor**-associated rejection antigen.

L56 ANSWER 33 OF 98 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 10
AN 94:110356 BIOSIS
DN 97123356
TI II. The B5 monoclonal human autoantibody **binds** to cell surface TNF-alpha on human lymphoid cells and cell lines and appears to recognize a novel epitope.
AU Boyle P; Lembach K J; Wetzel G D
CS Biol. Products, Pharmaceutical Div., Cellular Molecular Biol. Research, Miles Inc., P.O. Box 1986, Berkeley, CA 94701, SUA
SO Cellular Immunology 152 (2). 1993. 569-581. ISSN: 0008-8749
LA English
AB A human IgM monoclonal **antibody** (B5) recognizing human TNF-alpha was established from **peripheral blood lymphocytes** by transformation with Epstein-Barr virus and subsequent cell fusion. The B5 monoclonal **antibody** (mAb) **binds** to cell surface TNF-alpha (csTNF-alpha) on human T cells, **B cells**, and monocytes. In addition, this autoantibody **binds** to csTNF-alpha on a variety of lymphoid and monocyte lineage cell lines of human origin, as well as

astrocytomas, a breast **carcinoma**, and a melanoma. Interestingly, the B5 mAb also **binds** to chimpanzee lymphocytes and to mouse T lymphoma cell line csTNF-alpha. Many neutralizing mouse anti-TNF-alpha mAbs do not exhibit comparable **binding** to csTNF-alpha. This is consistent with the previous demonstration that B5 recognizes an epitope on TNF-alpha distinct from those recognized by three neutralizing mouse anti-TNF-alpha mAbs. B5 **binding** to csTNF-alpha is specific since it can be inhibited by TNF-alpha. No inhibition of B5 **binding** was seen by a neutralizing mouse anti-TNF-alpha mAb. The B5 autoantibody appears to recognize the transmembrane form of TNF-alpha and most likely also recognizes TNF-alpha associated with its receptor. The unique specificity of this B5 autoantibody provides some additional insight into the complex physiology of cell surface-associated TNF-alpha.

L56 ANSWER 34 OF 98 MEDLINE DUPLICATE 11
AN 93123740 MEDLINE
TI Endogenous secretion of IL-4 maintains growth and Thy-1 expression of a transformed B cell clone.
AU Louie S W; Ramirez L M; Krieg A M; Maliszewski C R; Bishop G A
CS Department of Microbiology, University of Iowa, Iowa City 52242.
NC AI28847 (NIAID)
DK252-95 (NIDDK)
SO J Immunol, (1993 Jan 15) 150 (2) 399-406.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9304
AB The CD5+ B cell lymphoma clone, CH12.LX, endogenously produces IL-4. Blocking the **binding** of this IL-4 to its cellular receptor inhibited the continuous **proliferation** of CH12.LX. mAb specific for either IL-4 or the IL-4R profoundly and specifically inhibited the **proliferation** of CH12.LX cells in a concentration-dependent manner, within 4 h after the addition of mAb. The addition of exogenous rIL-4 alone to CH12.LX cells had no effect on either **proliferation** or antibody secretion. However, exogenous rIL-4 was able to counteract the effects of anti-IL-4 antibody. Treatment of CH12.LX cells with antisense RNA oligodeoxynucleotides to IL-4 also specifically inhibited cell **proliferation** and decreased the levels of IL-4 secreted into the culture supernatants by more than 50%, without effect on total RNA or protein synthesis. Effects of antisense IL-4 were also blocked by addition of exogenous IL-4. Control oligodeoxynucleotides of equal size and base composition had no effect, and IL-4 antisense oligodeoxynucleotides did not effect the growth of a B cell lymphoma clone which does not produce IL-4. Blocking the **binding** of endogenously produced IL-4 to CH12.LX cells did not change the levels of membrane IL-4R or CD5 molecules. However, the constitutive expression of Thy-1 by these B cells was markedly decreased, and anti-Thy-1 antibodies decreased **proliferation** and

PMA-induced aggregation of CH12.LX cells. Autocrine secretion of IL-4 thus appears to be required both for the continuous **proliferation** of CH12.LX B cells, as well as their expression of Thy-1, which may function either as a homotypic adhesion molecule or a signal transduction molecule for these cells. These findings indicate that endogenously produced lymphokines may play a critical role in the maintenance of B cell hyperproliferative disorders.

L56 ANSWER 35 OF 98 LIFESCI COPYRIGHT 1996 CSA
AN 94:23032 LIFESCI
TI Expression of membrane receptor for **tumour** necrosis factor on human blood lymphocytes
AU Zola, H.; Flego, L.; Weedon, H.
CS Dep. Clin. Immunol., Flinders Med. Cent., Bedford Park, S.A. 5042, Australia
SO IMMUNOL. CELL BIOL., (1993) vol. 71, no. 4, pp. 281-288. ISSN: 0818-9641.
DT Journal
FS F
LA English
SL English
AB Using a monoclonal **antibody** against the human p75 **tumour** necrosis factor receptor (TNFR-I) combined with a high-sensitivity immunofluorescence flow cytometric procedure, a proportion of **peripheral blood lymphocytes** can be shown to express TNFR-I constitutively. The tonsil **B cells** which express TNFR-I include both cells with a germinal centre cell phenotype and cells with the phenotype of the follicular mantle zone. **Activation** of **B cells** with anti-immunoglobulin, alone or in combination with interleukin-4 or interleukin-2, increases receptor expression, particularly in cells with the phenotype of mantle zone cells. The functional significance of constitutive expression of TNFR by blood and tissue lymphocytes is discussed.

L56 ANSWER 36 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 93158144 EMBASE
TI **Peripheral blood lymphocytes** express the platelet-type thrombin receptor.
AU Howells G.L.; Macey M.; Curtis M.A.; Stone S.R.
CS Department of Oral Pathology, London Hospital Medical College, Turner Street, London E1 2AD, United Kingdom
SO BR. J. HAEMATOL., (1993) 84/1 (156-160). ISSN: 0007-1048 CODEN: BJHEAL
CY United Kingdom
DT Journal
FS 025 Hematology
LA English
SL English
AB Northern blot analysis of human mononuclear cells indicated that the platelet thrombin receptor may be expressed by lymphocytes. In order to investigate this, we prepared affinity purified rabbit

antibodies against the thrombin receptor which **bound** platelets and blocked thrombin **activation**. Using flow cytometry on peripheral blood cells, we found that the vast majority of NK cells (CD16/CD56 positive) and a fraction of CD3/CD4 positive T cells expressed the thrombin receptor. **B cells**, neutrophils and monocytes were negative. These data suggest that potentially thrombin may play a direct role in regulating NK and T cell function.

L56 ANSWER 37 OF 98 CANCERLIT
AN 93304506 CANCERLIT
TI Humoral and cellular immunopathology of hepatic and cardiac hamster-into-rat xenograft rejection. Marked stimulation of IgM++bright/IgD+dull splenic B cells.
AU Langer A; Valdivia L A; Murase N; Woo J; Celli S; Fung J J; Starzl T E; Demetris A J
CS Pittsburgh Transplant Institute, Department of Pathology, Pennsylvania.
SO Am J Pathol, (1993). Vol. 143, No. 1, pp. 85-98.
Journal code: 3RS. ISSN: 0002-9440.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; Cancer Journals; L; Priority Journals
LA English
OS MEDLINE 93304506
EM 9308
AB Normal Lewis rat serum contains antibodies (IgM > IgG) that **bind** to hamster leukocytes and endothelial cells. Transplantation of either the heart or liver from hamster rat results in release of hamster hematolymphoid cells from the graft, which lodge in the recipient spleen (cell migration), where recipient T- and B-cell populations initiate DNA synthesis within one day. There is marked stimulation of splenic IgM++(bright)/IgD+(dull) B cells in the marginal zone and red pulp, which account for 48% of the total splenic blast cell population by 4 days after liver transplantation. CD4+ predominant T-cell **proliferation** in the splenic periarterial lymphatic sheath and paracortex of peripheral lymph nodes occurs almost simultaneously. The effector phase of rejection in cardiac recipients is dominated by complement-fixing IgM antibodies, which increase daily and result in graft destruction in 3 to 4 days, even in animals treated with FK506. In liver recipients, combined antibody and cellular rejection, associated with graft infiltration by OX8+ natural killer, and fewer W3/25+ (CD4) lymphocytes, are responsible for graft failure in untreated recipients at 6 to 7 days. FK506 inhibits the T-cell response in liver recipients and significantly prolongs graft survival, but does not prevent the rise or deposition of IgM antibodies in the graft. However, a single injection of cyclophosphamide 10 days before transplantation effectively depletes the splenic IgM++(bright)/Ig+(dull) cells and in combination with FK506, results in 100% survival of both cardiac and hepatic xenografts for more than 60 days. Although extrapolation of morphological findings to functional significance is fraught with potential problems, we propose the following mechanisms of

xenografts rejection. The reaction initially appears to involve primitive host defense mechanisms, including an IgM-producing subpopulation of splenic B cells and natural killer cells. Based on the reaction and distribution of OX8+ and W3/25+ cells, antibody-dependent cell cytotoxicity and delayed-type hypersensitivity responses seem worthy of further investigation as possible effector mechanisms. Effective control of xenograft rejection is likely to require a dual pharmaceutical approach, one to contain T-cell immunity and another to blunt the primitive B-cell response.

L56 ANSWER 38 OF 98 CANCERLIT
AN 94697589 CANCERLIT
TI An immunotoxin, an **antibody**-drug conjugate and a heterodimeric **antibody** conjugate show **tumor**-specific efficacy in animal survival models (Meeting abstract).
AU Shah S A; Ferris C A; Derr S M; Bourret L A; Chari R V; Venkatesh Y P; Goldmacher V S; Lambert J M; Blattler W A
CS ImmunoGen Inc., 148 Sidney St., Cambridge, MA 02139
SO Antibody Immunoconjugates Radiopharmaceuticals, (1993). Vol. 6, No. 1, pp. 69.
ISSN: 0892-7049.
DT (MEETING ABSTRACT)
FS ICDB
LA English
EM 9404
AB The therapeutic efficacies of an immunotoxin, an **antibody**-drug conjugate and a heterodimeric **antibody** conjugate (with **activated** human **PBLs**) were assessed in xenograft mouse **tumor** models. Anti-CD19 monoclonal **antibody**, anti-B4, conjugated to blocked ricin (anti-B4-bR, 50 or 75 ug/kg/d iv x 5) was evaluated in SCID mice bearing 7 d established human **B-cell** lymphoma (4 x 10(6) Namalwa cells, iv). Controls included treatment with unconjugated anti-B4 **antibody** (2 mg/kg/d iv x 5) or a nonspecific **antibody**-blocked ricin conjugate (N901-bR, 100 ug/kg/d iv x 5). Anti-transferrin receptor **antibody**, 5E9, conjugated to a maytansinoid (5E9-Maytansinoid, 7 mg/kg/d, on days 1, 3, 5) was injected iv in SCID mice one hour after ip injection of A375 human melanoma cells (3.5 x 10(7)). Three iv injections of a mixture of unconjugated 5E9 **antibody** (15 mg/kg/d x 3) plus free maytansinoid drug (0.11 mg/kg/d x 3) served as a control. The **antitumor** efficacy of a heterodimeric conjugate, anti-B4-anti-T11(3) (1 mg/kg iv) together with IL2/anti-T3 **activated** human **PBLs** (1 x 10(7) cells/d iv x 3) was evaluated in the iv Namalwa model of SCID mice under different treatment protocols. Mice were injected iv with Namalwa cells (4 x 10(5)) and treated either 1 hr or 24 hr later with the heterodimeric conjugate. Beginning 24 hr after conjugate administration, both sets of animals were given 3 daily injections of **PBLs**. N901-anti-T11(3), which does not **bind** to the **tumor** cells, served as a control. All three **antibody** conjugates tested showed efficacy by significantly (p less than 0.05)

prolonging the life of animals, while no such effects were observed in the control groups. Calculations from cell titration curves indicated that up to 5.8 logs of **tumor** cells could be eliminated in vivo. These studies indicate that anti-B4-bR, 5E9-maytansinoid and anti-B4-anti-T11(3) heterodimer plus human **PBLs** have the potential to increase survival times and to effect complete cures in 25% of mice with malignant disease.

L56 ANSWER 39 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 92223982 EMBASE
TI CD5 is phosphorylated on tyrosine after stimulation of the T-cell antigen receptor complex.
AU Davies A.A.; Ley S.C.; Crumpton M.J.
CS Imperial Cancer Research Fund, Lincoln's Inn Field, London WC2A 3PX, United Kingdom
SO PROC. NATL ACAD. SCI. U. S. A., (1992) 89/14 (6368-6372).
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal
FS 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
AB When T cells are **activated** by the T-cell antigen receptor, a number of cellular proteins are phosphorylated on tyrosine. We investigated whether any of these proteins were present on the surface of **activated** T cells. Using the human leukemic T-cell line Jurkat and normal **peripheral blood lymphocytes**, we identified a 67-kDa cell surface glycoprotein in anti-phosphotyrosine immunoprecipitates, after treatment of the cells with CD3 **antibody**. When cell lysates were depleted of CD5 by sequential immunoprecipitation, the 67-kDa phosphotyrosyl polypeptide was no longer precipitated by the phosphotyrosine **antibody**. Western blot analysis of anti-phosphotyrosine precipitates confirmed that this glycoprotein was CD5. It was possible that CD5 was present in the anti-phosphotyrosine immunoprecipitates due to its physical association with phosphotyrosyl proteins rather than being directly tyrosine- phosphorylated itself. However, Western blot analysis of anti-CD5 immunoprecipitates with phosphotyrosine **antibody** and phosphoamino acid analysis demonstrated that CD5 was indeed phosphorylated on tyrosine after stimulation of the cells with CD3 **antibody** and was concomitantly phosphorylated on serine and threonine. Tyrosine phosphorylation of CD5 was maximal 2 min after CD3 stimulation and returned to baseline levels by 60 min. CD5 is expressed on the cell surface of all mature T cells and a small proportion of **B lymphocytes** and has recently been identified as the ligand for CD72, a receptor present on the surface of all **B cells**. The present data suggest that tyrosine phosphorylation may be involved in **B-cell**-T-cell communication.

L56 ANSWER 40 OF 98 MEDLINE DUPLICATE 12

AN 92112988 MEDLINE
TI **Activation**-dependent recognition by hematopoietic cells of the LDV sequence in the V region of fibronectin.
AU Wayner E A; Kovach N L
CS University of Minnesota, Department of Laboratory Medicine and Pathology, Minneapolis 55455.
NC HL-07093-16 (NHLBI)
SO J Cell Biol, (1992 Jan) 116 (2) 489-97.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9204
AB It has been shown that the alpha 4 beta 1 integrin is the lymphocyte receptor for the carboxy terminal cell-**binding** domain of fibronectin which comprises adhesion sites in Hep 2 and a high affinity site, CS-1, in the type III connecting segment or V (for variable) region. In the present studies, using a series of peptides derived from CS-1, we identify the tripeptide leu-asp-val (LDV), as the minimal peptide capable of supporting stable lymphocyte or melanoma cell adhesion. However, only cells which expressed an active form of the alpha 4 beta 1 complex were capable of attaching to and spreading on LDV peptide. On a molar basis, LDV minimal peptides were either not active or 10-20 times less active than intact CS-1 in promoting the adhesion of lymphocytes expressing the resting form of the receptor. In cells which express the high avidity form of the receptor, LDV and CS-1 were equally effective in promoting cell adhesion and spreading. The avidity of the alpha 4 beta 1 complex could be altered with mAbs to beta 1 which specifically **activate** beta 1 dependent function. The high avidity form of the alpha 4 beta 1 complex could be induced on U937 cells, T, and **B lymphoblastoid** cell lines, or PHA-stimulated T cell blasts. Resting **PBL** could not be induced to **bind** LDV peptide conjugates by **activating antibodies** to beta 1 implying that two signals are required for LDV recognition by T cells. In conclusion, these data show clearly that the minimal peptide for the alpha 4 beta 1 complex in CS-1 is the LDV sequence. Although numerous cell populations can interact with intact CS-1 only cells which express an active alpha 4 beta 1 complex can **bind** the LDV sequence. This implies that cell interaction with the carboxy terminal cell-**binding** domain of fibronectin can be regulated at several levels: (a) alpha 4 beta 1 expression; (b) **activation** of the alpha 4 beta 1 complex; and (c) alternate splicing of CS-1 into V+ isoforms of fibronectin.

L56 ANSWER 41 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 92168355 EMBASE
TI Adhesion of T and **B lymphocytes** to extracellular matrix and endothelial cells can be regulated through the .beta. subunit of VLA.
AU Van de Wiel-Van Kemenade E.; Van Kooyk Y.; De Boer A.J.; Huijbens

R.J.F.; Weder P.; Van de Kasteele W.; Melief C.J.M.; Figdor C.G.
CS Division of Immunology, Netherlands Cancer Institute, Antoni van Leeuwenhoek Huis, Plesmanlaan 121, 1066 CX Amsterdam, Netherlands
SO J. CELL BIOL., (1992) 117/2 (461-470).
ISSN: 0021-9525 CODEN: JCLBA3
CY United States
DT Journal
FS 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
AB Investigating the regulation of very late antigen (VLA)-mediated functions, we found that TS2/16, a mAb directed against the .beta. chain of the VLA group of integrins, can induce **binding** of resting **peripheral blood lymphocytes**, cloned T lymphocytes, and Epstein Barr virus-transformed **B cells** to extracellular matrix components, fibronectin, laminin, and collagen, but not to fibrinogen. The **antibody** stimulates VLA-4-, VLA-5-, and VLA-6-mediated **binding**. Furthermore, it induces VLA-4-mediated **binding** to vascular cell adhesion molecule-1 expressed by rTNF-.alpha.-stimulated endothelial cells, but it does not stimulate homotypic aggregation of cells as described for a number of anti-VLA-4.alpha. **antibodies** (Bednarczyk, J. L., and B. W. McIntyre. 1990. J. Immunol. 144:777-784; Campanero, M. R., R. Pulido, M. A. Ursa, M. Rodriguez- Moya, M. O. de Landazuri, and F. Sanchez-Madrid. 1990. J. Cell Biol. 110:2157-2165). Therefore, the stimulating **activity** of this anti-.beta.1 **antibody** clearly contrasts with that of the anti-VLA-4.alpha. **antibodies**, which induce homotypic cell aggregation, but not **binding** of cells to extracellular matrix, components or endothelial cells, indicating that TS2/16 may generate different signals. The observation that also F(ab')2 or Fab fragments of this anti-.beta.1 **antibody** stimulate **binding** to extracellular matrix components and endothelial cells excludes the possibility that **binding** requires receptor crosslinking, or is Fc receptor mediated. Induction of this adhesion is cation and energy dependent and requires an intact cytoskeleton. Although changes in the conformation of VLA integrins induced by this **antibody** may regulate their functional **activity**, the dependence on metabolic energy indicates that intracellular processes may also play a role.

L56 ANSWER 42 OF 98 CANCERLIT
AN 92379850 CANCERLIT
TI MONOCYTE-INDEPENDENT T-CELL **ACTIVATION** BY POLYCLONAL ANTITHYMOCYTE GLOBULINS.
AU Bonnefoy-Berard N; Vincent C; Verrier B; Revillard J P
CS Laboratory of Immunology, INSERM U80 CNRS URA1177 UCBL, Hopital E. Herriot, Lyon, France.
SO Cell Immunol, (1992). Vol. 143, No. 2, pp. 272-83.
Journal code: CQ9. ISSN: 0008-8749.
DT Journal; Article; (JOURNAL ARTICLE)

FS MEDL; Cancer Journals; L; Priority Journals
LA English
OS MEDLINE 92379850
EM 9211
AB The in vitro mitogenic properties of polyclonal antithymocyte and antilymphocyte globulins (ATG) on peripheral blood mononuclear cells were investigated. The ATG were mitogenic in a dose-dependent manner with maximal **proliferation** observed at 250 or 500 micrograms/ml. ATG **activated** blastogenesis of CD4+, CD8+, and CD57+ (NK cells) lymphocytes. The ATG induced interleukin-2 (IL-2) and interferon-gamma (IFN-gamma) gene expression and lymphokine secretion in cell culture supernatant and IL-2 receptor (CD25) expression. At submitogenic concentrations ATG potentialized the effect of phorbol esters on T cell **proliferation**, but not that of calcium ionophore. The mitogenic effect of ATG was not abrogated by monocyte depletion indicating that like CD2 monoclonal antibodies (mAbs) ATG **activate** T cells via a monocyte-independent pathway. CD3 and CD2 mAbs which **activate** T cells without **binding** to B surface determinants stimulated the **proliferation** of B cells and their differentiation into immunoglobulin (Ig)-secreting cells. In contrast, ATG induced only a transient B cell **activation**, but failed to support B cell differentiation into Ig-secreting cells despite the secretion of IL-2. These properties shared by ATG obtained in horses or rabbits by immunization with different cell types appear to differ from those of other T cell mitogens.

L56 ANSWER 43 OF 98 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 91-050947 [07] WPIDS
DNC C91-021650
TI New suppressor factor isolated from lymphoblastoid **tumour** cells - used for treating graft versus host disease, auto-immune disease, leukaemia and other malignancies.
DC B04
IN PLATSOUCAS, C
PA (SLOK) SLOAN KETTERING INST CANCER
CYC 1
PI US 4988676 A 910129 (9107)*
ADT US 4988676 A US 88-218620 880713
PRAI US 88-218620 880713
AN 91-050947 [07] WPIDS
AB US 4988676 A UPAB: 930928
Purified human suppressor factor is claimed which is isolated from human lymphoblastoid **tumour** cell supernatant where it is constitutively found and characterised by: (a) suppression of mitogen, antigen or alloantigen driven cellular proliferation of human peripheral blood leukocytes (**PBLS**), (b) suppression of **antibody** prodn., synthesis and secretion, (c) mol. wt. of 55,000-70,000 daltons, (d) suppression of cellular proliferative response of T and **B cells**, (e) suppression of cellular proliferative response driven by alloantigens, antigens and mitogens selected from Pokeweed mitogen (PWM), concanavalin A (conA) and phytohaemagglutinin (PHA), (f) inhibition of proliferative

response of human peripheral blood mononuclear leukocytes to allogeneic cells in mixed lymphocyte cultures, (g) inhibition of proliferation of **tumour** cell lines, (h) having no effect on natural killer cell cytotoxicity, (i) inhibition of **antibody** prodn. in vitro by human peripheral blood mononuclear leukocytes exposed to PWM, (j) not affecting the viability of human peripheral blood mononuclear leukocytes in culture, (k) not causing lysis of K-562 leukemic cell targets as detd. by chromium release assay and (l) not inducing the differentiation of suppressor T-cells.

USE - The suppressor factor (SF) can be used for treating or preventing graft versus host disease and also in patients who have received heterologous or autologous transplants. It can also be used in treating autoimmune diseases such as systemic lupus erythematosus, myasthenia gravis, rheumatoid arthritis, multiple sclerosis and allergies. The SF can also be used for the treatment of lympho-proliferative disorders such as leukemia as well as other malignancies including human solid **tumours** e.g. in the lung or colon.

0/3

L56 ANSWER 44 OF 98 CANCERLIT
AN 92084727 CANCERLIT
TI PROTEIN KINASE C (PKC) **ACTIVATION** VIA HUMAN LEUCOCYTE ANTIGEN CLASS II MOLECULES. A NOVEL REGULATION OF PKC ACTIVITY.
AU Brick-Ghannam C; Huang F L; Temime N; Charron D
CS Laboratoire d'Immunogenetique Moleculaire, Institut des Cordeliers, Paris, France.
SO J Biol Chem, (1991). Vol. 266, No. 35, pp. 24169-75.
Journal code: HIV. ISSN: 0021-9258.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; Cancer Journals; L; Priority Journals
LA English
OS MEDLINE 92084727
EM 9202
AB Analysis of intracellular localization of protein kinase C (PKC) in a lymphoblastoid B cell line shows that anti-human leucocyte antigen (HLA) class II antibodies induce an increase of cytosolic and membrane PKC activities. This phenomenon is both time- and dose-dependent. The maximal PKC **activation** was observed after exposure to 12.5 micrograms/ml antibody for 30 to 45 min. Unlike TPA, no translocation of the cytosolic PKC was observed at any time following exposure to the anti-HLA class II antibodies. We observed a good correlation between the [3H]phorbol dibutyrate **binding** activity and the enzymatic activity of PKC. Using a panel of antibodies specific for the HLA class II isotypes (DP, DQ, DR), we demonstrated that PKC **activation** via HLA class II molecules is not restricted to one isotype. We also showed by Western blot analysis that the increased PKC activity correlates with a quantitative increase of PKC. The increase of PKC activity induced by anti-HLA class II antibodies was completely abolished by the treatment with actinomycin D, a transcriptional inhibitor, or cycloheximide, a translational inhibitor. Finally, Northern blot

analysis revealed that anti-HLA class II antibodies induce an increase of the PKC alpha and PKC beta mRNAs levels which are significant after 20 min of stimulation and rose to a maximum after 60 min. In summary, our results show that increased PKC activity induced by HLA class II antibody is regulated at the transcriptional level.

L56 ANSWER 45 OF 98 CANCERLIT
AN 91170707 CANCERLIT
TI LIGATION OF MEMBRANE IG LEADS TO CALCIUM-MEDIATED PHOSPHORYLATION OF THE PROTO-ONCOGENE PRODUCT, ETS-1 [PUBLISHED ERRATUM APPEARS IN J IMMUNOL 1991 SEP 15;147(6):2068].
AU Fisher C L; Ghysdael J; Cambier J C
CS Department of Pediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, CO 80206.
NC AI20519
AI21768
AI00048
SO J Immunol, (1991). Vol. 146, No. 6, pp. 1743-9.
Journal code: IFB. ISSN: 0022-1767.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; Cancer Journals; L; Priority Journals
LA English
OS MEDLINE 91170707
EM 9105
AB Recent studies have demonstrated that the nuclear protein, Ets-1, which is preferentially expressed in lymphocytes, **binds** to the long terminal repeat of Moloney murine sarcoma virus and HTLV-1 and regulates gene expression. The association of Ets-1 with DNA has been shown to be lost when the protein is phosphorylated. Thus, Ets-1 may regulate gene expression in lymphocytes and this activity may be determined by its phosphorylation state. To address the possibility that Ets-1 activity may be altered by membrane (m) Ig-mediated signal transduction, we analyzed the effect of mIgM and mIgD ligation on the phosphorylation state of Ets-1. Monoclonal anti-IgM or anti-IgD antibody stimulation of normal mouse B cells led to increased phosphorylation of Ets-1 within 2 min. This response was absolutely dependent on calcium mobilization and could be induced by elevation of intracellular free calcium using the calcium ionophore, ionomycin. Calcium release from intracellular stores was sufficient to mediate the phosphorylation of Ets-1. Treatment of resting B cells with IL-4, TGF beta-1, IFN-gamma, anti-class I, or anti-class II antibodies did not induce Ets-1 phosphorylation. In summary, calcium mobilization from intracellular stores after mIgM or mIgD ligation provides a necessary and sufficient signal for **activation** of Ets-1 phosphorylation. This phosphorylation event may act in the alteration of gene expression during B cell **activation**.

L56 ANSWER 46 OF 98 CANCERLIT
AN 92679457 CANCERLIT
TI CLONAL **B CELLS** AND IMMUNOREGULATORY FUNCTIONS IN MONOCLONAL GAMMOPATHIES: AN IN VITRO IMMUNOLOGICAL STUDY.

AU Osterborg C A
CS Karolinska Institutet, Sweden
SO Diss Abstr Int [C], (1991). Vol. 52, No. 4, pp. 568.
ISSN: 0419-4217.
DT (THESIS)
FS ICDB
LA English
EM 9205
AB The **tumor** cell clone in monoclonal gammopathies (MG) is generally believed to comprise plasma cells in the bone marrow, but may also include peripheral blood **B lymphocytes** bearing identical idiotypic (id) immunoglobulin (Ig) surface structures as in the cytoplasm of the plasma cells. The presence of clonal **B cells** in the peripheral blood of patients (pts) with untreated multiple myeloma was found to be a strong predictor of prognosis. As a first attempt to characterize NK cells in human MG, NK cell functions in the peripheral blood of MG pts were studied and related to disease activity. A high NK activity and high numbers of cells with NK related cell surface markers were found in pts with a low **tumor** burden, whereas the NK functions were low in pts with advanced disease. An id-specific cellular and humoral immunity with regulatory influence on the myeloma **tumor** cell clone have been demonstrated in murine myeloma systems. Here, id-specific immunity in human MG was studied. The production of anti-id **antibodies** was analyzed from cell cultures of EBV-transformed **peripheral blood lymphocytes** of MG pts. A high anti-id production was found in pts with a low **tumor** burden. In pts with advanced disease, the anti-id production was low. The presence of id-**binding** T cells as well as T cell reactivity with a panel of TCR anti-V gene specific MAbs was studied. Three out of 11 tested pts had 1-15% id-**binding** CD4+ or CD8+ T cells in the peripheral blood. Three pts had a biased TCR V gene expression, but these T cell populations did not **bind** the id. T cell clones were isolated from repeatedly id-stimulated cultures of peripheral blood mononuclear cells from three pts with MG. In all three pts CD4+ or CD8+ T cell clones were obtained which **bound** to and showed a significant **proliferative** response to autologous id Ig. These results provide further support for MG as a differentiating **B cell** disorder. The cellular and humoral immunity against id Ig structures as well as NK cells might have a regulatory role on the **tumor** cell clone in MG. (Abstract shortened by UMI.)

L56 ANSWER 47 OF 98 CANCERLIT
AN 91205244 CANCERLIT
TI DIFFERENTIAL EFFECTS OF INTERFERON-GAMMA AND LOW MOLECULAR WEIGHT BCGF ON GROWTH OF HUMAN B LYMPHOCYTES; INTERFERON-GAMMA PROLONGS THE INCREASED C-MYC MRNA LEVELS AFTER **ACTIVATION**.
AU Lmo J; Smeland E B; Stokke T; Holte H; Funderud S; Blomhoff H K
CS Institute for Cancer Research, Norwegian Radium Hospital, Olso, Norway.
SO Scand J Immunol, (1991). Vol. 33, No. 4, pp. 365-73.

Journal code: UCW. ISSN: 0300-9475.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; Cancer Journals; L; Priority Journals
LA English
OS MEDLINE 91205244
EM 9106
AB We have characterized the growth-stimulating effect of Interferon-gamma (IFN-gamma) on various parameters of B cell growth, and compared the effects with those of low molecular weight B cell growth factor (lmw BCGF). We have found that IFN-gamma did not affect early changes induced by anti-mu, like initial calcium-flux and rise in mRNA-and protein levels of the proto-oncogene c-myc measured at 3 h. On the other hand, IFN-gamma enhanced the effect of anti-mu on parameters measured later in the G1 phase of the cell cycle, such as expression of the transferrin receptor and general transcriptional activity, measured as an increase in 7-aminoactinomycin D **binding**. In particular, whereas the c-myc levels in anti-mu-treated cells peaked at 3 h and then gradually declined, IFN-gamma together with anti-mu maintained the c-myc levels at 24 h at approximately the same levels as seen at 3 h. Overall, lmw BCGF had a more potent effect on the parameters affected by IFN-gamma, correlating with stronger enhancement of DNA synthesis. However, in contrast to IFN-gamma lmw BCGF did not affect anti-mu-induced c-myc mRNA levels. Thus this study has revealed differences between two B cell growth factors in effects on B cell cycle parameters.

L56 ANSWER 48 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 92268556 EMBASE
TI Anti-idiotypic immunity as a potential regulator in myeloma and related diseases.
AU Holm G.; Bergenbrant S.; Lefvert A.-K.; Yi Q.; Osterborg A.; Mellstedt H.
CS Department of Medicine, Karolinska Hospital, Box 60500, S-104 01 Stockholm, Sweden
SO ANN. NEW YORK ACAD. SCI., (1991) 636/- (178-183).
ISSN: 0077-8923 CODEN: ANYAA
CY United States
DT Journal
FS 025 Hematology
026 Immunology, Serology and Transplantation
LA English
SL English
AB In this paper some recent and partly preliminary results on anti-idiotypic immunity against clonal **B cells** in human monoclonal gammopathies are summarized. **B cell** lines producing **antibodies** to idiotypic determinants on autologous monoclonal immunoglobulin could be propagated after **activation** with Epstein-Barr virus of **peripheral blood lymphocytes** from patients with MGUS and MM clinical stage I but not from untreated persons with advanced MM. Blood T lymphocytes from patients with MGUS and Waldenstrom's macroglobulinemia were **activated** to

DNA synthesis and production of interleukins by the autologous M protein. In another series of experiments T cell clones raised from patients with MM clinical stage I and MGUS **bound** F(ab')2 fragments of the autologous M protein and were stimulated to DNA synthesis by the idiotope-bearing protein. Control experiments demonstrated the specificity for idiotypic determinants. Ten of eleven clones were CD4- /CD8+. Finally, using a panel of 8 mAbs to alpha/beta V region epitopes, we noted a clonal expansion of CD4+ and CD8+ T cells in MGUS and MM patients.

L56 ANSWER 49 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 91167340 EMBASE
TI In vitro studies of the effect of MAb NDA 4 linked to toxin on the **proliferation** of a human EBV-transformed lymphoblastoid **B cell** line and of gibbon MLA leukemia cell line.
AU Harris P.; Reed E.; King D.W.; Suciu-Foca N.
CS Department of Pathology, College of Physicians and Surgeons, Columbia University, 630 West 168th Street, New York, NY 10032, United States
SO CELL. IMMUNOL., (1991) 134/1 (85-95).
ISSN: 0008-8749 CODEN: CLIMB8
CY United States
DT Journal
FS 025 Hematology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
AB The rejection of allografts is mediated by cytolytic T cells and **antibody**-secreting **B cells**. Selective ablation of these **activated** cells from **peripheral blood lymphocytes** may offer a method of controlling allograft rejection. An immunotoxin was prepared from the monoclonal **antibody** (mAb) NDA 4, which recognizes a differentiation antigen (NDA 4) common to **activated** B and T cells. MAb NDA 4 was conjugated to the ribosome-inhibiting protein gelonin via a cleavable disulfide bond provided by a crosslinking reagent. The purified immunotoxin was evaluated for in vitro cytotoxicity on NDA 4 positive T and **B cell** lines. Conjugation of mAb NDA 4 to gelonin increased the in vitro cytotoxicity by a concentration factor of 1000, compared to gelonin alone. The specificity and saturability of mAb NDA 4 **binding**, as well as the number of antigenic sites per cell on resting versus **activated** T lymphocytes, were also evaluated. Resting T cells expressed 400-800 sites per cell. PHA-**activated** T cells and the MLA T cell leukemia expressed 10,000 to 80,000 sites per cell. Peripheral blood mononuclear cells obtained from allografted baboons in quiescence or undergoing rejection were compared for NDA 4 expression by flow cytometry. Lymphocytes obtained from baboons rejecting a heart allograft expressed NDA 4, whereas transplant recipients in quiescence showed no detectable NDA 4. These results suggest that mAb NDA 4-derived immunotoxins may be valuable for the selective depletion of **activated** lymphocytes while sparing the resting population.

L56 ANSWER 50 OF 98 BIOTECHDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 92-14295 BIOTECHDS
TI Production and application of human monoclonal **antibodies** ;
hepatitis B virus, Pseudomonas aeruginosa exotoxin-A monoclonal **antibody** production and bispecific **antibody** production via tetradoma construction (conference paper)
AU Iwasa S
CS Takeda-Chem.
LO Biology Research Laboratories, Takeda Chemical, Ltd., 2-17-85 Jusohonmachi 2-chome, Yodogawa-ku, Osaka 532, Japan.
SO Antibody Eng.; (1991) 9 pp.
DT Journal
LA English
AN 92-14295 BIOTECHDS
AB 5 Hybridomas secreting human monoclonal **antibodies** (MAbs) against hepatitis B virus surface antigen (HBsAg) and 1 hybridoma secreting a human MAb against Pseudomonas aeruginosa exotoxin-A (PEA) were formed by fusion of Epstein-Barr virus (EBV)-transformed **peripheral blood lymphocytes** with human **B-lymphoblastoid** cell line TAW-925. The hybridomas produced 0.5-3 ug/ml **antibody**.million cells.day for 6 mth. 4 Of the HBsAg MAbs exhibited 1.7-fold higher **antibody** (Ab) titer in an EIA using HBsAg-sensitized beads than human polyclonal Ab. The HBsAg-specific MAbs failed to protect chimpanzees from hepatitis B virus challenge, while the PEA-specific MAb neutralized in vitro cytotoxicity and in vivo lethal effects with 100- and 70-fold higher **activity** than serum polyclonal Abs, respectively. A hybrid hybridoma secreted a human bispecific MAb (BiMAb) recognizing human A431 epidermoid **carcinoma** cells and PEA. The tetradoma was isolated from unfused hybridomas by hydroxyapatite HPLC. Another BiMAb reactive with prourokinase (proU) and fibrin enhanced the thrombolytic **activity** of proU in a hamster pulmonary embolism model. (0 ref)

L56 ANSWER 51 OF 98 CANCERLIT
AN 91060941 CANCERLIT
TI EGR-1 EXPRESSION IN SURFACE IG-MEDIATED B CELL **ACTIVATION**. KINETICS AND ASSOCIATION WITH PROTEIN KINASE C **ACTIVATION**.
AU Seyfert V L; McMahon S; Glenn W; Cao X M; Sukhatme V P; Monroe J G
CS Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia 19104-6082.
NC AI23568
DK13914-20
SO J Immunol, (1990). Vol. 145, No. 11, pp. 3647-53.
Journal code: IFB. ISSN: 0022-1767.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; Cancer Journals; L; Priority Journals
LA English
OS MEDLINE 91060941
EM 9102

AB We have studied the expression of an immediate/early type gene, Egr-1, in murine B lymphocyte responses to Ag receptor-generated signals. The Egr-1 gene encodes a zinc finger protein with sequence-specific DNA **binding** activity and is believed to act as an intracellular "third messenger," to couple receptor-generated signals to **activation**-associated changes in gene expression. We show here that Egr-1 mRNA expression is rapidly and transiently (returning to basal levels by 6 h) induced after receptor crosslinking with anti-receptor antibodies. Egr-1 protein expression is more prolonged, maintaining detectable levels through 12 h. The induction of Egr-1 is a primary response to Ag receptor signaling, as it is independent of new protein synthesis and is inhibited by actinomycin D. We have also examined the linkage of Egr-1 to known signaling pathways associated with G0 to G1 transition by these cells in response to signals generated through the B cell Ag receptor. Egr-1 mRNA was not induced after elevation of intracellular free Ca2+. In contrast, the pharmacologic agents PMA and SC-9, which directly **activate** protein kinase C, both cause marked increases in Egr-1 mRNA levels with the same kinetics as observed after anti-receptor antibody stimulation. Further, the protein kinase C inhibitors H7, sangivamycin, and staurosporin block anti-receptor antibody-induced expression of Egr-1, thus, B cell Ag receptor-linked Egr-1 expression is likely coupled to the protein kinase C component of transmembrane signaling. Preliminary promoter mapping studies are consistent with this conclusion, because both PMA and anti-receptor antibody act through the same or overlapping cis-regulatory elements.

L56 ANSWER 52 OF 98 MEDLINE DUPLICATE 13
AN 90187862 MEDLINE
TI Regulation of B lymphocyte responses to IL-4 and IFN-gamma by **activation** through Ly-6A/E molecules.
AU Codias E K; Malek T R
CS Department of Microbiology and Immunology, University of Miami School of Medicine, FL 33101.
NC CA46096 (NCI)
SO J Immunol, (1990 Mar 15) 144 (6) 2197-204.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9006
AB The Ly-6 family of cell surface molecules has previously been shown to participate in T cell **activation**. We show that Ly-6A/E proteins also modulated the response of normal B lymphocytes in three separate in vitro assays. First, unfractionated or small resting B cells **proliferated** when cultured with IFN-gamma, IL-4, and an anti-Ly-6A/E mAb. Second, this anti-Ly-6A/E mAb restored B cell **proliferation** responses that were inhibited when coculturing the B cells in IFN-gamma, IL-4, and anti-IgM. Third, anti-Ly-6A/E specifically up-regulated the cell surface expression of its own Ag, and this response was dependent

upon co-stimulation with IFN-gamma. Mixing of T and B cells in culture suggested that T cells did not contribute substantially to the B cell **proliferative** response. Moreover, up-regulation of Ly-6A/E was observed for one B cell lymphoma, WEHI-231. Therefore, it appeared that modulation of B cell function by anti-Ly-6A/E was due to a direct effect of the mAb **binding** to the B cells. Taken together, these data suggest Ly-6A/E proteins are functional on B cells and may play a regulatory role in B cell **activation.**

L56 ANSWER 53 OF 98 CANCERLIT
AN 90663835 CANCERLIT
TI A MONOCLONAL **ANTIBODY** (5A6) THAT INHIBITS CELL GROWTH REACTS WITH A 26-KD CELL SURFACE PROTEIN NONCOVALENTLY ASSOCIATED WITH THE LEU-13 ANTIGEN (MEETING ABSTRACT).
AU Takahashi S; Doss C; Levy S; Evans R L; Levy R
CS Dept. of Medicine, Stanford Univ. Medical Center, Stanford, CA 94305
SO Proc Annu Meet Am Assoc Cancer Res, (1990). Vol. 31, pp. A1536. ISSN: 0197-016X.
DT (MEETING ABSTRACT)
FS ICDB
LA English
EM 9101
AB A monoclonal **antibody** was isolated by immunization with a human **B-lymphoma** cell line and screening for growth inhibition. This **antibody** reacted with most human cell lines tested, including those of hematolymphoid, neuroectodermal, and mesenchymal origin. It did not react with U937, a monocyte cell line. In peripheral blood, the **antibody** was reactive with all lymphoid cells, but very weakly or not at all with granulocytes and monocytes. The **antibody** induced cell aggregation of all cell lines to which it **bound**, but inhibited the growth of only a subset of these cell lines. The **antibody** also inhibited cell division of **PBL activated** by PHA or OKT3. The **antibody** immunoprecipitated a single chain protein of 26 kD from cell lysates made with Triton X-100, but additional proteins were precipitated when cell lysates made with CHAPS were used. We have identified one of these coprecipitated molecules as the 16-kD Leu-13 antigen. 5A6 and anti-Leu-13 showed similar, although not identical, reactivity, growth inhibition, and aggregation effects among hematolymphoid cell lines. These results suggest that the 26-kD molecule may play an important role in growth control.

L56 ANSWER 54 OF 98 MEDLINE DUPLICATE 14
AN 91109773 MEDLINE
TI Regulation of Fc gamma R II expression and function by B lymphocyte **activators.**
AU Laszlo G; Dickler H B
CS Experimental Immunology Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892.
SO Mol Immunol, (1990 Dec) 27 (12) 1189-93. Journal code: NG1. ISSN: 0161-5890.

CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9105
AB B lymphocytes cultured with LPS show increased expression of Fc gamma R II and increased **binding** of Ag-IgG complexes (both greater than 200%). In contrast, B lymphocytes cultured with either IL-4 or anti-mu show a marked loss (85-90%) of **binding** of Ag-IgG complexes that is specific, time and temperature dependent, and reversible. Decreased **binding** of complexes was not due to decreased expression of the receptor and therefore appears to be due to some form of alteration of the receptor. Based on the observation that the loss of **binding** of complexes requires protein synthesis, we favor the view that the loss is due to association of Fc gamma R II with another membrane molecule whose expression is induced or increased by IL-4 or anti-mu. Anti-mu induced loss of Fc gamma R II ligand **binding** capacity does not require cross-linking of surface IgM because the effect can be generated with F(ab') anti-mu. Anti-mu induced loss of Fc gamma R II **binding** of complexes was substantially prevented by IFN-gamma, whereas IFN-gamma did not reduce the anti-mu caused increase in expression of MHC class II molecules. This result shows that increased expression of the latter molecules can be dissociated from loss of Fc gamma R II ligand **binding** capacity. A myeloid cell line was identified that constitutively expresses Fc gamma R II **binds** relatively few complexes. This cell line may be useful in identifying alterations of Fc gamma R II which lead to the loss of **binding** of complexes. These results indicate that various B lymphocyte **activators** have different effects on B lymphocyte expression and function, and can thereby affect Fc gamma R II generated regulatory signals.

L56 ANSWER 55 OF 98 MEDLINE DUPLICATE 15
AN 91031155 MEDLINE
TI [The expression of an antigen interacting with monoclonal **antibody** IB4 on the surface membranes of normal human leukocytes and in lymphoproliferative diseases]. Izuchenie ekspressii antigena, vzaimodeĭstvuiushchego s monoklonal'nym antitelom IB4, na poverkhnostnykh membranakh leĭkotsitov cheloveka v norme i pri limfoproliferativnykh zabolevaniiakh.
AU Filatov A V; Bachurin P S; Sidorenko S P; Abramenko I V; Gluzman D F
SO Eksp Onkol, (1990) 12 (5) 40-3.
Journal code: EEC. ISSN: 0204-3564.
CY USSR
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals; Cancer Journals
EM 9102
AB Monoclonal **antibody** (MAb) 1B4 of IgG3 isotype reacting with 55 +/- 10% **peripheral blood lymphocytes** was obtained. MAb 1B4 is **bound** with

100% of B and NK cells and 50-70% of T cells in blood. The most part of CD8+ cells (60-100%) and approximately 50% of CD4+ cells belong to 1B4+ population. T-ALL cells do not express 1B4 antigen. Analysis of reactivity of MAb 1B4 with transformed malignant cells has shown that 1B4 antigen appeared in the process of differentiation of **B lymphocytes** at the state of pre-**B cells** and disappeared with **activation** of **B lymphocytes** and transition to plasma cells.

L56 ANSWER 56 OF 98 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 89-108381 [15] WPIDS
CR 84-220849 [36]; 94-233889 [28]
DNC C89-047955
TI New cytotoxic mono clonal **antibody** specific for **tumour** cells - and activated lymphocytes for treatment and diagnosis of solid **tumours**, leukaemia, transplant rejection, etc..
DC B04 D16
IN BILLING, R J
PA (BILL-I) BILLING R J
CYC 13
PI EP 311438 A 890412 (8915)* EN 16 pp
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
EP 311438 B1 941228 (9505) EN 18 pp
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
DE 3852601 G 950209 (9511)
ADT EP 311438 A EP 88-309398 881007; EP 311438 B1 EP 88-309398 881007; DE 3852601 G DE 88-3852601 881007, EP 88-309398 881007
FDT DE 3852601 G Based on EP 311438
PRAI US 87-115739 871008
AN 89-108381 [15] WPIDS
CR 84-220849 [36]; 94-233889 [28]
AB EP 311438 A UPAB: 940907
New cytotoxic monoclonal **antibody** (MAb) of class IgM, produced from a hybridoma made by fusing a mouse mycloma cell with spleen cells from a mouse immunised with leukaemia cells has the following properties; (1) reacts with almost all human solid **tumour** cells from freshly frozen tissue sections and cultured **tumour** cell lines; (2) reacts with almost all peripheral blood leukaemia cells of the lymphoid and myeloid subclasses; chronic myeloid leukaemia in the blast crisis phase and all T, B or mylloid lekaemia cell lines; (3) reacts with all PHA-activated lymphocytes and lymphocytes activated in the mixed lymphocyte culture reaction (A) reacts with some peripheral blood monocytes; (5) does not kill with complement, nor blind to the membrane of, normal peripheral blood T or **B lymphocytes** granulocytes, platelets and erythrocytes; and (6) does not react with normal somatic cells. Also new in the antigen (designated **cancer** associated growth factor, CAGF) against which MAb is directed.

USE/ADVANTAGE - MAb and CAGF, opt. when coupled to cytotoxic agents, are useful for treating solid timours; acute leukaemias; autoimmune diseases; transplant rejection and allergies. They can

also be used to detect/classify malignant cells and activated lymphocytes in body tissue (opt. when coupled to a radioisotope). Unlike known **antibodies** (e.g. OKT3), MAb reacts only with activated lymphocytes, not with lymphocytes which are not dividing to has no appreciable side effects.
0/9
Dwg.0/9

ABEQ EP 311438 B UPAB: 950207
A partially purified antigen of vertebrate source that has the following properties: (a) it functions as an autocrine growth factor produced by **tumour** cells and activated lymphocytes, (b) it binds to the surface membrane of **tumour** cells and stimulates the growth of these cells and cells of the lymphoid series, (c) it is present on the cell membrane and within the cytoplasm of **tumour** cells and activated lymphocytes, (d) it is present in the cytoplasm of unstimulated normal **peripheral blood lymphocytes** but when these cells are stimulated by antigens or by mitogens, said antigen appears also on cell membrane, (e) it is present on lymphocytes activated in vitro by mitogens, (f) its molecular weight is approximately 15,000 daltons, (g) it is capable of binding to CBL1 monoclonal **antibody** which is produced by the hybridoma cell line having ATCC number HB 8214.
Dwg.0/9

L56 ANSWER 57 OF 98 LIFESCI COPYRIGHT 1996 CSA
AN 89:63753 LIFESCI
TI Synergistic **antitumor** effects of interleukin 2 and the monoclonal Lym-1 against human Burkitt lymphoma cells in vitro and in vivo.
AU Gill, I.; Agah, R.A.; Hu, E.; Mazumder, A.
CS Norris Compr. Cancer Hosp., Rm. 624, 1441 Eastlake Ave., Los Angeles, CA 90033, USA
SO CANCER RES., (1989) vol. 49, no. 19, pp. 5377-5379.
DT Journal
FS F
LA English
SL English
AB Interleukin 2 (IL-2) regulates immune responses by inducing **proliferation** and differentiation of T-cells into cytotoxic cells, inducing lymphokine **activated** killer activity and enhancing **antibody** dependent cellular cytotoxicity (ADCC). Lym-1, a monoclona **antibody**, recognizes a membrane antigen present on the surface of **B-lymphoma** cells and can be used for ADCC. The authors therefore used Raji (human Burkitt lymphoma) cells to study the efficacy of combination therapy with IL-2, lymphokine **activated** killer activity, and Lym-1. In vitro ADCC assays using Lym-1 showed that preincubation of **peripheral blood lymphocytes** with IL-2 had a synergistic **antitumor** effect. In vivo experiments performed by growing Raji **tumors** in nude mice also demonstrated the increase in ADCC and the synergism between IL-2 and Lym-1 in terms of decreased **tumor** size and growth. The

mechanism of this synergy is probably from **activation** of cells mediating ADCC.

L56 ANSWER 58 OF 98 MEDLINE DUPLICATE 16
AN 89235136 MEDLINE
TI A role for class I MHC antigens in responses of **activated** B lymphocytes.
AU Southern S O; Dutton R W
CS Department of Biology, University of California, San Diego, La Jolla 92093.
NC PO AI-23287
AI-08795
SO J Immunol, (1989 May 15) 142 (10) 3384-91.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8908
AB Expression of the H-2 D protein was increased over 10-fold in B cells **activated** by IL-4 IL-5, IFN-gamma or LPS. Differences in the regulation of H-2 D expression and in growth rates were detected during lymphokine-triggered responses of subpopulations of splenic B cells. The enhancement of H-2 D expression on **activated** B cells was regulated at the transcriptional level and required synthesis of an intermediate cellular protein(s). B cell growth and differentiation were inhibited by antibodies to the H-2 D Ag suggesting a signaling function for the class I molecules on **activated** B lymphocytes. In T cells, a similar elevation of H-2 D expression occurred after stimulation with IL-5 or Con A.

L56 ANSWER 59 OF 98 CANCERLIT
AN 89381359 CANCERLIT
TI DIFFERENTIAL REGULATION OF MURINE B CELL FC GAMMA RII EXPRESSION BY CD4+ T HELPER SUBSETS.
AU Snapper C M; Hooley J J; Atasoy U; Finkelman F D; Paul W E
CS Department of Pathology, Uniformed Services University of the Health Sciences, Bethesda, MD 20814.
SO J Immunol, (1989). Vol. 143, No. 7, pp. 2133-41.
Journal code: IFB. ISSN: 0022-1767.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; Cancer Journals; L; Priority Journals
LA English
OS MEDLINE 89381359
EM 8911
AB The murine B cell FcR for IgG (Fc gamma RII) is a membrane glycoprotein reported to mediate inhibition of B cell **activation** and differentiation. We show that IL-4 inhibits the enhanced expression of Fc gamma RII by LPS-stimulated B cells. This activity is completely reversed by anti-IL-4 mAb and is specific, in that multiple other lymphokines tested do not exert a similar effect. This effect of IL-4 is apparent by day 1 of culture,

although maximal inhibition occurs on day 4 at a concentration of 500 U/ml. The IL-4-induced inhibition of enhanced Fc gamma RII expression by LPS stimulation observed on day 4 of culture is associated with a significant reduction in the steady state level of Fc gamma RII beta gene-specific mRNA. IFN-gamma which inhibits many of the effects of IL-4 on B cells, does not reverse the IL-4-induced inhibition of Fc gamma RII membrane expression nor the levels of beta gene-specific mRNA. Fc gamma RII expression is significantly increased in B cells stimulated with antigen-specific, CD4+ T cell clones of the Th1 type (i.e., IL-2 and IFN-gamma-producing). By contrast, three different Th2 clones (i.e., IL-4-producing) fail to stimulate an increase in Fc gamma RII levels. Anti-IL-4 mAb significantly enhanced Fc gamma RII expression by Th2-stimulated B cells indicating that IL-4 was the active, inhibitory, substance produced by the Th2 cells. Supernatants from stimulated Th2 clones inhibited the enhanced expression of Fc gamma RII by LPS-stimulated B cells and this activity was completely reversed by anti-IL-4 mAb. By contrast, supernatants from stimulated Th1 clones further enhanced Fc gamma RII expression by LPS-stimulated B cells. The differential regulation of B cell Fc gamma RII expression by Th subsets may play an important role in the regulation of humoral immunity by altering the sensitivity of B cells to IgG immune complex-mediated inhibition of B cell **activation** and differentiation in vivo.

L56 ANSWER 60 OF 98 MEDLINE DUPLICATE 17
AN 89381312 MEDLINE
TI Cognate interactions between helper T cells and B cells. III. Contact-dependent, lymphokine-independent induction of B cell cycle entry by **activated** helper T cells.
AU Noelle R J; McCann J; Marshall L; Bartlett W C
CS Department of Microbiology, Dartmouth Medical School, Hanover, NH 03755.
NC GM-36814
GM37767
SO J Immunol, (1989 Sep 15) 143 (6) 1807-14.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8912
AB An Ag-specific, IL-2-dependent Th clone induced the growth of B cells in a class II-restricted, Ag-specific, IL-2-dependent manner. The formation of stable Th-3.1-B cell conjugates was restricted by Ag and class II MHC. After **activation** of Th-3.1 by insolubilized anti-T3 (Th-3.1T3), Th-3.1T3 induced the growth of B cells in a class II unrestricted, Ag nonspecific manner. The formation of stable conjugates between Th-3.1T3 and B cells was also class II unrestricted and Ag nonspecific. Although the interaction of Th-3.1T3 and B cells was class II unrestricted, the interaction was inhibited by the combination of anti-IA and anti-IE mAb. This suggested that monomorphic domains of class II MHC molecules were

involved in Th-3.1T3-B cell interaction. Fixed Th-3.1T3 but not fixed resting Th-3.1 induced B cell cycle entry, as measured by an increase in B cell RNA synthesis. Trypsin-treatment of Th-3.1T3 before fixation reduced their ability to **activate** B cells, indicating that cell surface proteins on Th-3.1T3 were required for enhanced B cell RNA synthesis. Anti-IL-4, anti-IL-2R, or anti-IFN-gamma did not affect the ability of Th-3.1T3 to induce heightened B cell RNA synthesis. Progression into S phase by B cells **activated** with fixed Th-3.1T3 was supported by the addition of soluble factors. When stimulated with fixed Th-3.1T3, EL4 supernatant (SN) enhanced B cell DNA synthesis. Depletion of IL-4, but not IL-2, from EL4 SN ablated its supportive capabilities. IL-4 alone was completely ineffective in supporting entry into S phase. Therefore, IL-4 and another activity(ies) in EL4 SN were necessary for B cell cycle progression into S phase. Taken together, these data suggest that after Th **activation**, Th cell surface proteins are expressed that mediate the **binding** of Th to B cells via recognition of nonpolymorphic domains of class II MHC molecules. Contact of Th-3.1T3 with B cells, not lymphokines, results in the entry of B cells into the cell cycle and heightened B cell lymphokine responsiveness. The addition of exogenous lymphokines supports the progression of Th-3.1T3-**activated** B cells into S phase.

L56 ANSWER 61 OF 98 LIFESCI COPYRIGHT 1996 CSA
AN 89:87737 LIFESCI
TI Persistent superphosphorylation of leukosialin (CD43) in **activated** T cells and in **tumour** cell lines.
AU Axelsson, B.; Perlmann, P.
CS Dep. Immunol., Biol. Build. F5, Univ. Stockholm, S-106 91 Stockholm, Sweden
SO SCAND. J. IMMUNOL., (1989) vol. 30, no. 5, pp. 539-547.
DT Journal
FS F
LA English
SL English
AB CD43 (leukosialin) is a highly sialylated, single-chain molecule expressed on most human leucocytes. Regulatory signals appear to be transduced through the molecule as suggested by the ability of anti-CD43 **antibodies** to induce aggregation and **proliferation** of T cells and to enhance **B-cell proliferation** and natural killer cell activity. **Activation** of protein kinases is an essential event in signal transduction. We were therefore interested to study whether CD43 may function as a substrate for protein kinases during mitogenic **activation** of lymphocytes. We show that CD43 was rapidly superphosphorylated (within minutes) on serine residues following addition of phorbol ester (PMA) to **peripheral blood lymphocytes**. The results suggest that CD43 has an important role during both early and late phases of T-cell **activation** and that modulation of its biochemical properties by protein kinases may be associated with progression through the cell cycle and with cellular growth.

L56 ANSWER 62 OF 98 CANCERLIT
AN 91137504 CANCERLIT
TI INTERFERON-GAMMA INHIBITS THE **PROLIFERATION** BUT NOT THE DIFFERENTIATION OF MURINE B CELLS IN RESPONSE TO IL-5.
AU Hitoshi Y; Mita S; Tominaga A; Kikuchi Y; Sonoda E; Takatsu K; Watanabe Y
CS Department of Biology, Kumamoto University Medical School, Japan.
SO Int Immunol, (1989). Vol. 1, No. 2, pp. 185-90.
Journal code: AY5. ISSN: 0953-8178.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; L; Priority Journals
LA English
OS MEDLINE 91137504
EM 9104
AB Interferon-gamma (IFN-gamma) is supposed to be produced by type 1 helper T cells (TH1) and inhibits IL-4-dependent B cell growth and differentiation. IL-5 (T cell-replacing factor, TRF), is a T cell-derived lymphokine which is predominantly produced by type 2 helper T cells (TH2) and regulates **proliferation** and differentiation of **activated** B cells. In this study, the effect of IFN-gamma on IL-5-dependent B cell growth and differentiation has been studied using murine chronic B cell leukemic cells (BCL1), normal splenic B cells, and cloned early B cell line. IFN-gamma selectively inhibits the IL-5-mediated **proliferation** of **activated** B cells as well as cloned early B cell lines at a low concentration (2 U/ml) in which polyclonal IgM production was not affected. This inhibitory effect of IFN-gamma occurs within 24 h after the onset of culture, as demonstrated by the inability of antibody to IFN-gamma to reverse totally the IFN-gamma-mediated suppressive effects if it was added later than 24 h after the onset of the culture. On the contrary, IL-5-mediated IgM secretion of BCL1 and IgA formation of LPS-stimulated normal B cells were relatively resistant to the suppressive effect of IFN-gamma. IFN-gamma does not affect the receptor expression for IL-5. Interestingly, IL-4-mediated IgG1 formation of LPS-stimulated B cells was markedly suppressed by IFN-gamma at 10 U/ml. These results strongly suggest that IFN-gamma may have differential effects on IL-5-mediated B cell triggering.

L56 ANSWER 63 OF 98 CANCERLIT
AN 89656588 CANCERLIT
TI ABNORMAL INTERLEUKIN 2 RECEPTOR EXPRESSION IN ADULT T CELL LEUKEMIA.
AU Uchiyama T
CS First Div., Dept. of Internal Medicine, Faculty of Medicine, Kyoto Univ., Kyoto 606, Japan
SO Non-serial, (1988). Interleukin 2. Smith KA, ed. New York, Academic, p. 179-96, 1988.
DT Book; (MONOGRAPH)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
FS ICDB
LA English

EM 8910
AB Interleukin 2 (IL-2), a polypeptide growth factor, was originally found as a T-cell growth-promoting factor. Specific **binding** sites for IL-2 were first demonstrated by a **binding** assay utilizing radiolabeled IL-2. Anti-Tac antibody was made by immunizing a mouse with T cells cultured with IL-2 from a patient with adult T-cell leukemia (ATL). Development of the anti-Tac monoclonal antibody, identification of anti-Tac antibody as an anti-IL-2 receptor antibody, characterization of IL-2 receptor (IL-2R), IL-2R expression in B cells, IL-2R expression in ATL, and human T-lymphotropic virus (HTLV) infection and IL-2R expression are described; and the possible role of IL-2R in the leukemogenesis and IL-2R expression in T-cell chronic lymphocytic leukemia are discussed. The anti-Tac antibody was shown to recognize human IL-2R by several pieces of evidence, including the inhibition of **binding** of IL-2, enabling cloning of the cDNA encoding the IL-2R. IL-2R is abnormally (constitutively) expressed on leukemic cells from ATL patients and cell line cells infected with HTLV-I, an etiologic agent of ATL. A hypothetical model of the leukemogenesis of ATL is presented that includes the following steps: (1) HTLV-I infection, (2) **activation** of the IL-2R gene, (3) constitutive expression of IL-2Rs, (4) polyclonal growth of T4(+) HTLV-I(+) cells through IL-2R (autocrine or paracrine), (5) selective and monoclonal growth of T4(+) HTLV-I(+) cells expressing IL-2Rs, and (6) development of ATL. (63 Refs)

L56 ANSWER 64 OF 98 MEDLINE
AN 89009688 MEDLINE
TI Human recombinant IL-4 induces **activated** B lymphocytes to produce IgG and IgM.
AU Defrance T; Vanbervliet B; P`ene J; Banchereau J
CS UNICET, Laboratory for Immunological Research, Dardilly, France.
SO J Immunol, (1988 Sep 15) 141 (6) 2000-5.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8901
AB In this report, we describe a novel biologic activity of IL-4 namely, its ability to induce **activated** human B cells to produce IgM. Staphylococcus aureus Cowan I-**activated** blasts prepared from high density tonsil B cells were found to secrete IgG and IgM, but no IgE, when cultured in the presence of rIL-4. The differentiating activity of rIL-4 was totally blocked by a neutralizing anti-IL-4 antiserum, therefore demonstrating that the IgG/IgM-inducing activity of rIL-4 was an intrinsic property of IL-4. rIL-4 was only minimally inducing Ig production of blasts prepared from low density B cells, whereas it induced B cell blasts prepared from high density B cells to secrete a high amount of Ig. Delayed additions of the neutralizing anti-IL-4 antiserum demonstrated that a 48-h contact between IL-4 and B cell blasts was required for optimal Ig production. The IL-4-mediated IgG and IgM

production was neither suppressed by IFN-gamma nor by anti-CD23 mAb 25, whereas these agents have been shown earlier to inhibit IgE production of enriched B cells cultured in the presence of IL-4. These data indicate that the IgG/IgM-inducing activity of IL-4 is not regulated like the IL-4-induced IgE production by enriched B cells.

L56 ANSWER 65 OF 98 CANCERLIT
AN 89009685 CANCERLIT
TI IFN-GAMMA AND PROSTAGLANDIN E2 INHIBIT IL-4-INDUCED EXPRESSION OF FC EPSILON R2/CD23 ON B LYMPHOCYTES THROUGH DIFFERENT MECHANISMS WITHOUT ALTERING **BINDING** OF IL-4 TO ITS RECEPTOR.
AU Galizzi J P; Cabrillat H; Rousset F; Menetrier C; de Vries J E; Banchereau J
CS UNICET, Laboratory for Immunological Research, Dardilly, France.
SO J Immunol, (1988). Vol. 141, No. 6, pp. 1982-8.
Journal code: IFB. ISSN: 0022-1767.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; Cancer Journals; L; Priority Journals
LA English
OS MEDLINE 89009685
EM 8812
AB Human rIL-4 specifically induces the expression of the low affinity receptor for IgE (Fc epsilon R2/CD23) on normal B cells and on the Burkitt lymphoma cell line Jijoye. IL-4 does not induce the generation of the second messenger cAMP in Jijoye cells. PGE2 (at 10(-7) M) was found to inhibit by 50% the IL-4 mediated Fc epsilon R2/CD23 induction on Jijoye cells. The PGE2 half maximum inhibitory concentration (1 nM) was comparable to that inducing a half maximal increase of intracellular cAMP (4nM PGE2). 8-bromo-cAMP (10(-3) M), forskolin (10(-5) M), and cholera toxin (100 ng/ml), which increase intracellular cAMP levels, also inhibited by 40 to 80% the IL-4 induced Fc epsilon R2/CD23 expression on Jijoye cells. PGE2 8-bromo-cAMP, forskolin, and cholera toxin also inhibited the IL-4-induced Fc epsilon R2/CD23 expression on normal B lymphocytes. Taken together these data suggest that PGE2 inhibits the IL-4 induced Fc epsilon R2/CD23 through an increase of intracellular cAMP. In contrast, IFN-gamma, which strongly inhibits IL-4-mediated Fc epsilon R2/CD23 expression on Jijoye cells, did not increase intracellular cAMP levels and thus probably acts through another mechanism. IFN-gamma and PGE2 did not inhibit **binding** of IL-4 to its receptor. It could be excluded that IFN-gamma and PGE2 were acting via an alteration/desensitization of the IL-4R inasmuch as 24 h pre-incubation of Jijoye cells with these agents affected neither the affinity of 125I-IL-4 for its receptor (Kd = 0.8 to 1.5 x 10(-10) M) nor the maximal number of **binding** sites per Jijoye cells (Bmax = 390 to 550). Furthermore, IFN-gamma and PGE2 did not affect the internalization and degradation of 125I-IL-4. These data demonstrate that PGE2 and IFN-gamma inhibit the IL-4-mediated induction of Fc epsilon R2/CD23 on B lymphocytes via different mechanisms that do not alter the interaction of IL-4 with its receptor.

L56 ANSWER 66 OF 98 LIFESCI COPYRIGHT 1996 CSA
AN 88:104458 LIFESCI
TI Western blot analysis of antigens on melanoma cells recognized by cytotoxic T cells.
AU Hersey, P.; MacDonald, M.; Werkman, H.
CS Immunol. and Oncol. Unit, 4th Fl., David Maddison Clin. Sci. Build., Royal Newcastle Hosp., Newcastle, N.S.W. 2300, Australia
SO J. NATL. CANCER INST., (1988) vol. 80, no. 11, pp. 826-835.
DT Journal
FS F
LA English
SL English
AB Antigens recognized by cloned cytotoxic T lymphocytes (CTLs) from patients with melanoma were examined by methods based on the ability of antigens immobilized on nitrocellulose paper to stimulate **proliferation** of the CTLs. The **proliferative** response depended on the presence of histocompatible antigen-presenting cells (APCs) in the cultures in the form of either autologous lymphoid cell lines (Epstein-Barr virus-transformed **B cells**) or histocompatible **peripheral blood lymphocytes** and was maximal at 3 days. Presentation appeared to be via class II major histocompatibility complex antigens, in that monoclonal **antibodies** (MAbs) against the class II antigens, but not the class I antigens, on the APCs inhibited the **proliferative** responses. The antigen(s) responsible for the stimulation were shown in all instances to have a molecular mass of 48 kilodatons. Preliminary analysis suggested that the antigen(s) have both protein and glycolipid (ganglioside) components.

L56 ANSWER 67 OF 98 CANCERLIT
AN 88270524 CANCERLIT
TI T- AND B-CELL-DERIVED SUPERNATANT FACTORS ENHANCE IGE SYNTHESIS BY A MYELOMA CELL LINE (U-266).
AU Ray A; Rocklin R E
CS Department of Medicine, New England Medical Center, Boston, Massachusetts 02111.
SO Cell Immunol, (1988). Vol. 114, No. 2, pp. 293-306.
Journal code: CQ9. ISSN: 0008-8749.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; Cancer Journals; L; Priority Journals
LA English
OS MEDLINE 88270524
EM 8809
AB IgE synthesis by the human myeloma line U-266 was enhanced 3- to 15-fold in the presence of supernatants from cultures of mononuclear cells (MNC). The enhancing activity was concentration-dependent and was derived from cells that were cultured in the absence of serum and received no in vitro stimulation by exogenous mitogens or lymphokines. T- and B-lymphocyte-enriched populations isolated from MNC were found to generate the enhancing activity, but no enhancing activity was produced by monocytes. MNC from atopic and nonatopic donors were equally effective as sources for this activity. The

enhancement of IgE synthesis was proportionally greater than the effect of the activity on cell **proliferation**. Furthermore, this enhancement of IgE synthesis was demonstrated to be isotype-specific in that the factor(s) had no effect on IgM- and IgG-secreting cell lines. It is suggested that augmentation of IgE synthesis by B cells at a late stage of differentiation may be accomplished by lymphokines constantly present in the cells' milieu and that the U-266 model may be useful for testing putative IgE regulatory factors.

L56 ANSWER 68 OF 98 CANCERLIT
AN 87310264 CANCERLIT
TI EFFECT OF TUMOR NECROSIS FACTOR ALPHA ON MITOGEN-**ACTIVATED** HUMAN B CELLS.
AU Kehrl J H; Miller A; Fauci A S
CS Laboratory of Immunoregulation, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20892.
SO J Exp Med, (1987). Vol. 166, No. 3, pp. 786-91.
Journal code: I2V. ISSN: 0022-1007.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; Cancer Journals; L; Priority Journals
LA English
OS MEDLINE 87310264
EM 8711
AB In this study we demonstrate that the monocyte/macrophage product, tumor necrosis factor alpha (TNF-alpha), has significant in vitro effects of B cell function. It costimulated with anti-mu in the induction of B cell DNA synthesis, and it prolonged the DNA synthesis initiated in B cell cultures stimulated with the human B cell mitogen, Staphylococcus aureus Cowan strain I (SAC). The addition of either IL-1 or IFN-gamma to TNF-alpha resulted in a substantial further increase in DNA synthesis. The addition of TNF-alpha to IL-2, a known inducer of SAC-**activated** B cell Ig secretion, resulted in a twofold enhancement in the amount of IL-2 stimulated B cell Ig secretion. Receptor **binding** studies with 125I-TNF-alpha demonstrate a marked increase in TNF-alpha **binding** sites after B cell **activation** (approximately 6,000 sites per cell, with an apparent Kd of 2.0 X 10(-10) M). Thus, TNF-alpha may be an important factor in human B cell function and is likely to interact with other T cell and monocyte derived cytokines in the regulation of human B cell **proliferation** and Ig production.

L56 ANSWER 69 OF 98 MEDLINE DUPLICATE 18
AN 87252247 MEDLINE
TI Inhibition of B lymphocyte **activation** by interferon-gamma.
AU Reynolds D S; Boom W H; Abbas A K
NC AI22802
CA09141
AI07451
SO J Immunol, (1987 Aug 1) 139 (3) 767-73.
Journal code: IFB. ISSN: 0022-1767.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8710
AB Helper/inducer T cell clones specific for protein antigens and class II MHC determinants consist of two nonoverlapping subsets. One (called Th1) secretes IL 2 and IFN-gamma and the other (Th2) produces BSF1 upon stimulation with antigen or polyclonal **activators**. By using hapten-**binding** normal B cells and the B lymphoma line WEHI-279 as assays for B cell helper (maturation) factors, we have shown that Th2 clone supernatants (SN) induce differentiation to antibody secretion, whereas Th1 SN do not. The failure of Th1 SN to **activate** B cells is due to inhibitory effects of IFN-gamma, because it can be reversed by a neutralizing monoclonal antibody specific for IFN-gamma. Thus, in the presence of this antibody, even Th1 SN stimulate B cell maturation maximally. Conversely, recombinant IFN-gamma inhibits **proliferation** and differentiation of B cells induced by active Th2 SN. These results demonstrate that IFN-gamma is a potent inhibitor of B lymphocyte **activation** and can be distinguished from growth and maturation-inducing helper factors that are produced by both subsets of helper T cells.

L56 ANSWER 70 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 87216096 EMBASE
TI Thyrotrophin receptor blocking **antibodies**: Incidence, characterization and in-vitro synthesis.
AU Kraiem Z.; Lahat N.; Glaser B.; Baron E.; Sadeh O.; Sheinfeld M.
CS Endocrine Research Unit, Carmel Hospital, Haifa 34362, Israel
SO CLIN. ENDOCRINOL. (OXFORD), (1987) 27/4 (409-421).
ISSN: 0300-0664 CODEN: CLENAO
CY United Kingdom
FS 003 Endocrinology
026 Immunology, Serology and Transplantation
LA English
AB The prevalence and characteristics of TSH receptor blocking **activity** were examined in patients with different thyroid disorders. Studies were also performed on the in-vitro synthesis and immunoregulation of the blocking **antibody**. Blocking **activity** was tested by measuring the inhibition of TSH-stimulated cAMP production of cultured human thyroid cells by patient immunoglobulin (Ig) preparations. The following patients were investigated (number of cases in parentheses): Hashimoto's thyroiditis (33); primary myxoedema (17); euthyroid ophthalmopathy (8); **active** Graves' disease (19); cold nodule (5); non-toxic goitre (14); toxic adenoma (8); toxic multinodular goitre (9) and 22 normal controls. TSH receptor blocking **activity** was only detected in primary hypothyroidism with the following characteristics: (i) Such **activity** was present in only 16% of the patients (both goitrous, i.e. Hashimoto's thyroiditis, and non-goitrous, i.e. primary myxoedema), and in three patients with previously **active** Graves' hyperthyroidism who had become hypothyroid. (ii) Blocking **activity** seems to be associated

with the Ig fraction of serum as indicated by protein A adsorption. (iii) The block-positive samples did not **bind** 125I-TSH, which seems to rule out an **antibody** directed against TSH. (iv) The specificity of the blocking **activity** seems to be directed towards the TSH-(thyroid stimulating immunoglobulin, TSI) receptor-mediated cAMP response since no inhibition of prostaglandin E1-stimulated cAMP production was found. Moreover, all cases in which an inhibitory effect was demonstrated towards TSH also exhibited blocking of TSI-stimulated cAMP, with a high correlation between the degree of inhibition of the TSH to that of the TSI response ($r=0.89$, $P<0.001$, $n=11$). The blocking **activity** may contribute to the pathogenesis of some cases of primary hypothyroid autoimmune thyroiditis, both goitrous and non-goitrous, as well as in the evolution of hyper- to hypothyroidism. By culturing **peripheral blood lymphocytes**, as well as B/T lymphocyte co-cultures isolated from three patients with blocking **activity** present in serum, the in-vitro synthesis of the blocking **antibody** was demonstrated for the first time. Moreover, in-vitro secretion of the **antibody** by patients **B lymphocytes**, as well as T cell regulation of autoantibody production, were also shown.

L56 ANSWER 71 OF 98 MEDLINE DUPLICATE 19
AN 87092374 MEDLINE
TI Selective killing of T lymphocytes by phototoxic liposomes.
AU Yemul S; Berger C; Estabrook A; Suarez S; Edelson R; Bayley H
SO Proc Natl Acad Sci U S A, (1987 Jan) 84 (1) 246-50.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8704
AB Two-fold specificity in drug delivery obtained through the localized **activation** of drugs by physical means and the attachment of drugs to proteins that **bind** to target cells might be used for highly selective **cancer** chemotherapy or for immunosuppression. Toward this end, a monoclonal **antibody** against an antigen on the surface of T lymphocytes was covalently attached to liposomes containing a phototoxic drug, pyrene, **bound** to the lipid bilayer. When unfractionated **peripheral blood lymphocytes**, or B- and T-cell lines, were irradiated after treatment with these liposomes, T cells were killed while **B cells** were spared, demonstrating the validity of the approach in a simple in vitro assay.

L56 ANSWER 72 OF 98 BIOTECHDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 86-07944 BIOTECHDS
TI Infinite **proliferation** of human monoclonal **antibody**-producing cells;
by coculture of human **B cell** strain carrying Epstein-Barr virus and blood reticular cells producing

immunoglobulin; application to diagnosis and therapy
PA Asahi-Chem.Ind.
PI JP 61067482 7 Apr 1986
AI JP 84-189622 12 Sep 1984
PRAI JP 84-189622 12 Sep 1984
DT Patent
LA Japanese
OS WPI: 86-128925 [20]
AN 86-07944 BIOTECHDS
AB The infinite **proliferation** of human monoclonal **antibody**-producing (or immunoglobulin-producing) cells is effected by coculture of (a) human **B-cell** strain carrying Epstein-Barr virus (EBV) gene and (b) blood reticular cells containing immunoglobulin-producing cells. Human monoclonal **antibody** to human pathogenic virus, **cancer**, HLA-antigen or autoimmunogenic autohistogenetic compoent may be obtained with ease, and the **antibody** obtained is useful for diagnosis or treatment of the relevant diseases. Preferred (a) is **B-cell** strain RPMI 1788 or HAT-sensitive **B-cell** strain (ATCC CRL 8118). Examples of (b) are **peripheral blood lymphocyte** fraction, lymph node cell fraction or spleen cell fraction. Suitable culture media for the coculture are not specifically limited, and RPMI 1640 containing 5-20% fetal calf serum (FCS) is preferred. An example describes incubation of EBV gene-carrying human **B-cell** strain CRL 8118 with lymph node cells from a stomach **cancer** using HAT medium containing 20% FCS for 14 days. The supernatant of the coculture was then reacted with KATO-III cell strain. (4pp)

L56 ANSWER 73 OF 98 MEDLINE DUPLICATE 21
AN 86087259 MEDLINE
TI Distinction of B cell maturation factors from lymphokines affecting B cell growth and viability.
AU Sherris D I; Sidman C L
NC CA-35845
AI-20232
SO J Immunol, (1986 Feb 1) 136 (3) 994-8.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8604
AB Supernatants from S26.5 helper T cells, autoimmune viable motheaten (mev/mev) mouse spleen cells, EL4 lymphoma cells, and recombinant DNA-derived interferon gamma (IFN-gamma), all of which display B cell maturation factor (BMF) activity, were assayed for effects on B cell **proliferation** alone and with Dextran Sulfate (DxS) and anti-immunoglobulin antibodies (alpha-Ig). Both EL4 and S26.5 supernatants showed BCGF-II (DxS co-stimulator) activity, whereas only EL4 supernatant had BCGF-I (alpha-Ig co-stimulator or BSF-I) activity. Supernatants from mev/mev spleen cells and recombinant

DNA-derived IFN-gamma showed no activity in either assay. Fractionation of S26.5 supernatant by chromatofocusing showed a divergence of BMF activity (BMF-T, pIa of 6.0) from BCGF-II activity (pIa of 5.4), providing evidence for their physical nonidentity. IFN-gamma, which decreases B cell viability in culture, was separable from BMF-T by phenyl-Sepharose chromatography. BMF-T from S26.5 supernatant was separated from IFN-gamma and BCGF-II and was shown to induce B cell maturation without affecting B cell **proliferation**. The molecular characteristics of the purified BMF-T were pIa 6.0, Mr 55,000 by G-75 gel filtration, and Mr 16,000 by SDS-PAGE. These data demonstrate that several lymphokines (BMF) exist that mediate the maturation of B cells to active Ig secretion without stimulating B cell **proliferation**.

L56 ANSWER 74 OF 98 CANCERLIT
AN 87627822 CANCERLIT
TI CHARACTERIZATION OF SOLUBLE SUPPRESSOR FACTORS PRODUCED BY UNSTIMULATED NORMAL HUMAN LYMPHOCYTES.
AU Schwartz S A; Nair M P
CS Dept. of Pediatrics, The Univ. of Michigan, Ann Arbor, MI
SO Non-serial, (1985). Mechanisms of Cytotoxicity by NK Cells. Herberman RB, Callewaert DM, eds. New York, Academic Press, p. 453-64, 1985.
DT (MEETING PAPER)
FS ICDB
LA English
EM 8701
AB Activities of soluble suppressor factors (SSF), their preliminary characterization, and the immunopharmacologic modulation of natural killer (NK) cells are described. When lymphocytes were cultured in serum-free medium, a potent SSF capable of inhibiting the **proliferative** responses of T cells and polyclonal **B cell activation** was consistently found in the supernatant fluid. SSF appears to be the product of an autologous mixed lymphocyte reaction, because neither T nor non-T cells alone were capable of its synthesis. SSF also could suppress the NK and **antibody**-dependent cell cytotoxicity (ADCC) activities of allogeneic lymphocytes. SSF inhibition of NK activity could be blocked by alpha-methyl-D-mannoside, L-fucose, and L-mannose, in a dose-dependent manner. These results suggest that SSF may act through **binding** to unique glycosylated residues on the surface of effector cells. In other experiments, amphotericin B and corticosteroids were shown to directly inhibit NK and ADCC activities, interleukin-2 (IL-2) was shown to suppress production of SSF, treatment of SSF with the enzymes chymotrypsin and trypsin was shown to suppress cytotoxicity (K562 target cells), and irradiation of **peripheral blood lymphocytes** was shown to decrease SSF production and NK cytotoxicity (K562 targets). In **cancer** patients and **tumor**-bearing animals, an abnormal increase in serum SSF may result in decreased immune surveillance and exacerbation of disease. In vitro experiments indicate that biological modifier substances such as interferon or IL-2 may have therapeutic potential in reversing abnormal suppressor

activity accompanying several disease states. (22 Refs)

L56 ANSWER 75 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 85226031 EMBASE
TI Generation of **tumor** cell-reactive human monoclonal **antibodies** using **peripheral blood lymphocytes** from **actively** immunized colorectal **carcinoma** patients.
AU Haspel M.V.; McCabe R.P.; Pomato N.; et al.
CS Litton Institute of Applied Biotechnology, Rockville, MD 20850-4373, United States
SO CANCER RES., (1985) 45/8 (3951-3961).
CODEN: CNREA8
CY United States
LA English
AB The use of human monoclonal **antibodies** (MCA) in the detection and treatment of human **cancer** has been limited by the apparent scarcity of MCA to **tumor** cell surface antigens. Using **peripheral blood lymphocytes** from autologous **tumor**-immunized patients, we isolated 36 mCA that react to sections of colorectal **carcinoma**. Twenty of these human MCA appear to be directed against cell surface antigens. Two-thirds of the human MCA-producing cell lines were diploid human **B-cells** rather than human-mouse heterohybridomas. Direct **antibody-binding** assays performed with the MCA indicated that they recognized antigenic determinants preferentially expressed on **tumor** cells. Experiments with paired specimens of air-dried, dissociated colon **tumor** cells and normal colonic mucosa cells suggested that the MCA **bound** significantly more to the cell surfaces of **tumor** cells than to the surfaces of normal colonic mucosa cells. Similarly, tests with a panel of cryostat sections of paired colon **tumor** and normal colonic mucosa showed that MCA **bound** to the **tumor** cells and not to the normal colonic mucosa. None of the MCA **bound** to cells from frozen sections of normal breast, stomach, liver, skeletal muscle, or skin. Furthermore, the human MCA did not react with **carcinoembryonic** antigen and human erythrocyte antigens as measured by various techniques. Our data also demonstrated that these transformed **B-cells** and hybridomas were stable producers of human MCA. Thus, our studies show that these **tumor**-specific human MCA may have the specificity and stability necessary for in vivo evaluation of their use in the detecion and treatment of **cancer**.

L56 ANSWER 76 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 86007078 EMBASE
TI Antiproliferative monoclonal **antibodies**: Detection and initial characterization.
AU Vaickus L.; Levy R.
CS Division of Hematology/Oncology, Department of Medicine, University of Iowa Hospitals and Clinics, Iowa City, IA 52242, United States
SO J. IMMUNOL., (1985) 135/3 (1987-1997).

CODEN: JOIMA3
CY United States
LA English
AB Two monoclonal **antibodies** (MAB) are described which inhibit in vitro cellular **proliferation** in the absence of complement or effector cells. These MAB were produced by hybridomas made from mice immunized against human **B lymphoma** cells. The MAB were detected by using a colorimetric assay that quantifies **proliferation** based on the conversion of a yellow tetrazolium salt to a purple formazan product, a reaction that occurs only in metabolically **active** cells with intact mitochondrial enzymes. A human **B lymphoblastoid** cell was used as the screening target. RBC4 is an IgM MAB that modulates and immunoprecipitates the transferrin receptor. RBG5 is an IgG1 that **binds** to a nonmodulating cell surface determinant different from the transferrin receptor. Both MAB are **active** at low concentrations (RBC4, 0.5 .mu.g/ml and RBG5, 0.01 .mu.g/ml). Immunofluorescence staining of cell lines by RBC4 and RBG5 shows little correlation with inhibition by the **antibodies**. They differentially inhibit the **proliferation** of a panel of T, B, and myeloid cell lines. Both **antibodies** inhibit the **proliferation** of alloantigen or mitogen-**activated** human **peripheral blood lymphocytes** (**PBL**). Unstimulated **PBL** are not affected by either MAB. The RB MAB each cause different morphologic changes of target cells. Whereas RBC4-inhibited cells exhibit nonspecific changes, RBG5 causes a progressive increase in the size and nuclear number of a subset of inhibited cells.

L56 ANSWER 77 OF 98 MEDLINE DUPLICATE 22
AN 85106243 MEDLINE
TI TCGF (IL 2)-receptor inducing factor(s). I. Regulation of IL 2 receptor on a natural killer-like cell line (YT cells).
AU Yodoi J; Teshigawara K; Nikaido T; Fukui K; Noma T; Honjo T; Takigawa M; Sasaki M; Minato N; Tsudo M; et al
SO J Immunol, (1985 Mar) 134 (3) 1623-30.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8505
AB A continuous cell line (YT cells) with inducible receptor for T cell growth factor (TCGF)/interleukin 2 (IL 2) was established from a 15-yr-old boy with acute lymphoblastic lymphoma and thymoma. YT cells were tetraploid, having 4q+ chromosomal markers, and **proliferated** continuously in vitro without conditioned medium (CM) or IL 2. They were weakly positive for OKT9, OKT11, and Tac antigen (Ag), a determinant closely associated with the receptor for IL 2 (IL 2-R), and were negative for OKT1, OKT3, OKT4, and OKT8 Ag. YT cells also expressed HNK-1 Ag and Fc receptors for IgG, which are expressed on natural killer (NK) cells. They retained a killing

activity against human cell lines, including K562 (myeloid), T, and **B cell** lines. Unlike Tac Ag/IL 2-R(+) cell lines derived from adult T cell leukemia (ATL), YT cells were negative for HTLV, as proved by Southern blotting with cDNA for viral DNA. The expression of Tac Ag was markedly enhanced in 18 hr, when YT cells were incubated with CM from PHA-stimulated peripheral blood leukocytes (**PBL**) or spleen cells, as determined by immunofluorescence by using flow cytometry and **binding** assay with 125I-anti-Tac **antibody** (Ab). The **binding** study with 125I-labeled recombinant IL 2 showed 3.2 X 10(4) IL 2 receptor sites on YT cells precultured with CM. PHA-P and Con A neither agglutinate nor enhance the expression of IL 2-R/Tac antigen on these non-T cell line cells. Furthermore, neither recombinant IL 2 nor gamma-interferon could induce IL 2-R on YT cells, suggesting the presence of a unique IL 2-R inducing factor in **PBL** or spleen CM. Unlike Tac Ag on HTLV(+), ATL-derived cell lines (Hut-102, MT-1, ATL-2), the expression of Tac Ag on YT cells was down-regulated by anti-Tac Ab. The induction of Tac Ag/IL 2-R on YT cells seemed specific, because the enhancement of Tac Ag expression was not associated with that of Ia Ag and T9/transferrin receptor.

L56 ANSWER 78 OF 98 MEDLINE DUPLICATE 23
AN 85124415 MEDLINE
TI Two mouse monoclonal **antibodies** detecting two different epitopes of an **activated** lymphocyte antigen on adult T-cell leukemia cells.
AU Ueda R; Nishida K; Koide Y; Tsuge I; Seto M; Yoshida M; Miyoshi I; Ota K; Takahashi T
SO Cancer Res, (1985 Mar) 45 (3) 1314-9.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8506
AB Mouse monoclonal **antibodies** were produced against MT-2 cell line derived from adult T-cell leukemia or human T-cell leukemia virus-rich fraction therefrom. Two IgG1 **antibodies**, Ta60a and Ta60b, were found to be reactive not only with cell lines derived from adult T-cell leukemia or cutaneous T-cell lymphomas, but also with **activated peripheral blood lymphocytes**, suggesting the similarity of Ta60 antigen group to Tac antigen which is present on interleukin 2 receptor. Thus, the relationship among these antigens was studied. Two Ta60 **antibodies** and Tac **antibody** immunoprecipitated the molecule with almost identical electrophoretic mobility, approximately a Mr 60,000 antigen from [3H]glucosamine-labeled **activated peripheral blood lymphocytes** or MT-2, MT-1, or ATN-1 cells from adult T-cell leukemia and a Mr 53,000 antigen from HUT-102 cells derived from cutaneous T-cell lymphomas. Further, Tac **antibody** was found to immunoprecipitate Ta60b molecule on

125I-labeled MT-2 cells by sequential immunoprecipitation, indicating that these two epitopes are on the same molecule. **Antibody binding** inhibition assays with either 3H-labeled Ta60a or Ta60b **antibody** demonstrated that Ta60a and Tac are the same epitope, but different from Ta60b. Thus, at least two epitopes were demonstrated to be present on interleukin 2 receptor molecule. However, Ta60b **antibody** showed almost no blocking effects on **proliferation** of an interleukin-2-dependent cell line, whereas Ta60a **antibody** did. Various hematopoietic **tumor** cells were typed with these two **antibodies**, but the results with Ta60b **antibody** were described, because they showed a similar specificity. Ta60b **antibody** reacted with all adult T-cell leukemia cases, but did not react with T-cell acute lymphoblastic leukemia, lymphoblastic lymphoma, or mature T-cell lymphoma. Interestingly, 3 of 12 acute myeloblastic leukemia and 2 of 5 chronic myelocytic leukemia in blastic crisis showed positive reactions. One-third of **B-cell** chronic lymphocytic leukemia and **B-cell** lymphoma as well as a few **B-cell** lines were also weakly reactive with this **antibody**. A part of the results with direct tests was confirmed by the absorption tests. The results obtained demonstrated the presence of Ta60b on a certain fraction of malignant hematopoietic cells of other than T-cell origin.

L56 ANSWER 79 OF 98 MEDLINE DUPLICATE 24
AN 85184578 MEDLINE
TI Obligatory role of gamma interferon in T cell-replacing factor-dependent, antigen-specific murine B cell responses.
AU Brunswick M; Lake P
SO J Exp Med, (1985 May 1) 161 (5) 953-71.
Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8508
AB The role of gamma interferon (IFN-gamma) in T cell-replacing factor (TRF) activity for antigen-specific plaque-forming cell (PFC) responses in vitro was studied using antibodies to murine IFN-gamma (Mu IFN-gamma). TRF activity was present in supernatants (Sn) of Con A- or mixed leukocyte reaction-stimulated murine spleen cells as well as in an IL-2-rich fraction of phytohemagglutinin-stimulated human peripheral blood lymphocyte Sn and in the Sn of the Gibbon T lymphoma MLA-144. The human TRF was highly active with cells from nu/nu mice and normal mice but not with cells from animals with the xid immunologic defect, similar to the activity of murine TRF. Antibodies to IFN-gamma consisted of hyper-immune rabbit antisera, IFN-gamma affinity-purified rabbit immunoglobulin and an interspecies hybridoma specific for Mu IFN-gamma. The results show that the activities of all preparations of TRF are markedly diminished or abrogated by antibody to Mu IFN-gamma but not by antibodies to human IFN-gamma (Hu IFN-gamma), nor by normal rabbit

sera or purified rabbit Ig. The degree of inhibition was dose dependent and was quantitatively reversed by the addition to the cultures of recombinant-derived Mu IFN-gamma (Mu rIFN-gamma) but not Hu rIFN-gamma. This reversal was fully antigen specific and thus not attributable to polyclonal B cell **activation** by IFN-gamma, which is inactive alone in the TRF assay. Kinetic analysis shows that IFN-gamma must act by 24-48 h to produce PFC responses at 4 d. Together, the data demonstrate that IFN-gamma is a necessary mediator for TRF effects and that IFN-gamma is induced by TRF from T-depleted murine spleen cells in sufficient quantity to support large antibody responses. The source of this IFN-gamma may be the potent natural killer cells that are induced in cultures stimulated with TRF.

L56 ANSWER 80 OF 98 BIOTECHDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 86-00176 BIOTECHDS
TI Human monoclonal **antibodies** in experimental **cancer** research;
hybridoma generation and monoclonal **antibody** production
AU Olsson L
LO Cancer Biology Laboratory, State University Hospital (Rigshospitalet), DK-2100 Copenhagen, Denmark.
SO J.Natl.Cancer Inst.; (1985) 75, 3, 397-403
CODEN: JNCIAM
DT Journal
LA English
AN 86-00176 BIOTECHDS
AB Very few established human myeloma cell lines have been reported, and thus has been an obstacle to the production of human hybridomas. Only a few are true myeloma cell lines, most being Epstein-Barr virus transformed lymphoblastoid cell lines. Human hybridomas may also be produced by the fusion of the mouse myeloma cells with human lymphocytes. In vitro priming systems seem to be the only realistic possibility in providing antigen-specific **B-lymphocytes**. Using **peripheral blood lymphocytes**, specific hybridoma **antibodies** against histones have been produced. DNA recombinant human monoclonal **antibody**, autochtonous **tumors**, oncogenes, an anti-idiotype approach, antigenic modulation, intramural intratumoral phenotypic diversity and metastatic **activity** and human monoclonal **antibodies** in the clinical management of **neoplastic** diseases are also discussed. (81 ref)

L56 ANSWER 81 OF 98 BIOTECHDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 84-08831 BIOTECHDS
TI Constitutive production of a suppressor factor by human T-T cell hybridomas;
hybridoma construction by fusion of Con A-**activated peripheral blood lymphocytes** with cells from lymphoblastoid human leukocytes (conference abstract)
AU Platsoucas C D; Calvelli T A; Kunicka J E; Lawless B D; Higgins J A

LO Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.
SO Fed.Proc.Fed.Am.Soc.Exp.Biol.; (1984) 43, 6, 1605
CODEN: FEPRA7
DT Journal
LA English
AN 84-08831 BIOTECHDS
AB Human T-T cell hybridomas were developed by fusing Con A-**activated** peripheral blood T lymphocytes with cells from lymphoblastoid human T cell lines (Jurkat or Molt-4). Hybrids were selected by a combination of cloning in agar and limiting dilution methods, without employing HAT medium. Several human T-T cell hybrids producing **B-cell** growth factor (BCGF) constitutively or after induction, were obtained using this approach. However, these hybrids ceased producing BCGF within a period of two months. Furthermore, human T-T cell hybrids constitutively producing a non-specific suppressor factor were also produced. These hybrids are stable. This suppressor factor exhibits the following properties: (1) suppresses the **proliferative** responses of T cells to allogeneic cells in mixed lymphocyte culture and to mitogens (PHA, Con A and PWM); (2) suppresses **antibody** production by peripheral blood mononuclear leukocytes in the PWM-induced system; (3) is not cytotoxic to humn lymphocytes or to cells from certain hemopoietic **tumor** cell lines; (4) does not affect natural killer cytotoxicity. (0 ref)

L56 ANSWER 82 OF 98 BIOTECHDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 84-11035 BIOTECHDS
TI Two new monoclonal **antibodies** (L-N-1 LN-2) reactive in B5 formalin-fixed paraffin-embedded tissues with follicular center and mantle zone human **B lymphocytes** and derived **tumors**;
construction of a hybridoma secreting monoclonal **antibody**
AU Epstein A L; Marder R J; Winter J N; Fox R I
LO Medical Oncology Section, North-western University Medical Center, 303 East Chicago Avenue, Chicago, IL 60611, USA.
SO J.Immunol.; (1984) 133, 2, 1028-36
CODEN: JOIMA3
DT Journal
LA English
AN 84-11035 BIOTECHDS
AB 2 Monoclonal **antibodies**, LN-1 and LN-2, reactive with **B lymphocytes** in B5 formaldehyde-fixed, paraffin-embedded tissue sections were produced using cell extracts from pokeweed mitogen-stimulated **peripheral blood lymphocytes** and diffuse histiocytic lymphoma SU-DHL-4 cells respectively. 3 10-Wk old BALB/c female mice were injected s.c. at multiple sites and 2 wk later the mice were reinoculated. 10 Days later, the mice received a 3rd i.p. injection of antigen, and 4 days later the spleens were removed and spleen cells were fused with 8-azaguanine-resistant mouse myeloma NS-1 cells using 40% polyethylene glycol 1,540. Culture supernatants from wells with

active hybridoma cell growth were tested by immunofluorescence and positive cultures were cloned on Noble agar containing RPMI 1640 medium, fetal calf serum and antibiotics. LN-1 and LN-2 stained cell lines of **B cell** lineage and their **binding** characteristics were analyzed. LN-1 and LN-2 are useful for diagnosis and classification of human lymphomas and leukemias. (34 ref)

L56 ANSWER 83 OF 98 MEDLINE DUPLICATE 25
AN 84088934 MEDLINE
TI Cloned human cytotoxic T lymphocyte (CTL) lines reactive with autologous melanoma cells. I. In vitro generation, isolation, and analysis to phenotype and specificity.
AU de Vries J E; Spits H
SO J Immunol, (1984 Jan) 132 (1) 510-9.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8404
AB **Activation** of **peripheral blood lymphocytes** (**PBL**) from a melanoma patient either in secondary MLC in which EBV-transformed **B cells** from the cell line JY were used as stimulator cells, or by co-cultivation with the autologous melanoma cells in a mixed leukocyte **tumor** cell culture (MLTC) resulted in the generation of cytotoxic activity against the autologous melanoma (O-mel) cells. From these **activated** bulk cultures four cloned cytotoxic T lymphocyte (CTL) lines were isolated. The CTL clone O-1 (T3+, T4+, T8-, OKM-1-, HNK-, and HLA-DR+), and O-36 (T3+, T4-, T8+, OKM-, HNK-, and HLA-DR+) were obtained from MLC, whereas the CTLC clones O-C7 (T3+, T4+, T8-, OKM-1-, HNK-, and HLA-DR+) and O-D5 (T3+, T4-, T8+, OKM-1-, HNK, and HLA-DR+) were isolated from autologous MLTC. All four CTL clones were strongly cytotoxic for O-mel cells but failed to lyse autologous fibroblasts and autologous T lymphoblasts. Moreover, the CTL clones lacked NK activity as measured against K562 and Daudi cells. Panel studies indicated that the CTL clones also killed approximately 50% of the allogeneic melanoma cells preferentially, whereas the corresponding T lymphoblasts were not lysed. Monoclonal **antibodies** against class I (W6/32) and class II (279) MHC antigens failed to block the reactivity of the CTL clones against O-mel and allogeneic melanoma cells, indicating that a proportion of human melanoma cells share determinants that are different from HLA antigens and that are recognized by CTL clones. In contrast to the CTL clones isolated from MLTC, the clones obtained from MLC also lysed JY cells, which initially were used as stimulator cells. The reactivity of O-36 against JY could be inhibited with W6/32, demonstrating that this reactivity was directed against class I MHC antigens. These results suggest that the lysis of O-mel and JY cells by O-36 has to be attributed to two independent specificities of this CTL clone. The specificity of the other cross-reactive CTL clone (O-1) could not be

determined. The notion that individual CTL clones can have two specificities was supported by the following observations. The cytotoxic reactivity of both O-1 (T4+) and O-36 (T8+) against JY was blocked by monoclonal **antibodies** directed against T3 and human LFA-1, and against T3, T8, and human LFA-1, respectively.(ABSTRACT TRUNCATED AT 400 WORDS)

L56 ANSWER 84 OF 98 BIOTECHDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 84-04834 BIOTECHDS
TI Cloned human cytotoxic T lymphocyte (CTL) lines reactive with autologous melanoma cells: I. in vitro generation isolation and analysis to phenotype and specificity;
analysis using monoclonal **antibodies**
AU De Vries J E; Spits H
LO Division of Immunology, The Netherlands Cancer Institute Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands.
SO J.Immunol.; (1984) 132, 1, 510-19
CODEN: JOIMA3
DT Journal
LA English
AN 84-04834 BIOTECHDS
AB **Activation** of **peripheral blood lymphocytes** (**PBL**) from a melanoma patient either in secondary mixed leukocyte culture (MLC) in which Epstein-Barr virus (EBV)-transformed **B cells** from the cell line JY were used as stimulator cells, or by co-culture with the autologous melanoma cells in a mixed leukocyte **tumor** cell culture (MLTC) resulted in the generation of cytotoxic **activity** against the autologous melanoma (0-mel) cells. From these **activated** bulk cultures, 4 cloned cytotoxic T lymphocyte (CTL) lines (O-1, O-36, O-C7 and O-D5) were isolated. Monoclonal **antibodies** against surface molecules expressed on CTL clones or on human O-mel were used to study the specific recognition structures associated with the ineraction of cloned CTL with autologous and allogeneic O-mel. SPV monoclonal **antibodies** were produced by hybridomas constructed by fusing SP 2/0 O-mel with spleen cells from mice immunized with the T8+ CTL clone HG-31 or with the T4+ CTL clone HG-38. The reactivity of the **antibodies** was examined and the results indicate that it is feasible to obtain CTL clones which kill autologous and allogeneic melanoma cells preferentially. (51 ref)

L56 ANSWER 85 OF 98 LIFESCI COPYRIGHT 1996 CSA
AN 84:57204 LIFESCI
TI Multiple myeloma: Circulating lymphocytes that express plasma cell antigens.
AU Ruiz-Argueelles, G.J.; Katzmann, J.A.; Greipp, P.R.; Gonchoroff, N.J.; Garton, J.P.; Kyle, R.A.
CS Mayo Clin./Found., Rochester, MN 55905, USA
SO BLOOD., (1984) vol. 64, no. 2, pp. 352-356.
DT Journal
FS F
LA English

SL English
AB The bone marrow and peripheral blood of 14 patients with multiple myeloma were studied with murine monoclonal **antibodies** that identify antigens on plasma cells (R1-3 and OKT10). **Peripheral blood lymphocytes** expressing plasma cell antigens were found in six cases. Five of these cases expressed the same antigens that were present on the plasma cells in the bone marrow. Patients that showed such peripheral blood involvement were found to have a larger **tumor** burden and higher bone marrow plasma cell **proliferative** activity. In some patients, antigens normally found at earlier stages of **B cell** differentiation (B1, B2, and J5) were expressed by **peripheral blood lymphocytes** and/or bone marrow plasma cells.

L56 ANSWER 86 OF 98 BIOTECHDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 84-05578 BIOTECHDS
TI Generation of anti-tetanus toxoid human monoclonal **antibodies**; construction of a hybridoma secreting monoclonal **antibody** (conference abstract)
AU Freimark B; Ozer H
LO Department of Medical Oncology, Roswell Park Memorial Institute, Buffalo, NY 14263, U.S.A.
SO Hybridoma; (1984) 3, 1, 86
CODEN: HYBRDY
DT Journal
LA English
AN 84-05578 BIOTECHDS
AB A variety of mouse monoclonal **antibodies** are employed as diagnostic reagents and several are currently undergoing Phase I clinical trials, but human monoclonal **antibodies** may prove superior for clinical applications. The purpose of this study was to define the optimal conditions required to reproducibly generate stable human-human hybridomas from peripheral blood **B cells**. Of 15 human **tumor** cell lines screened to yield hybrids only 1, UC-729-6, produced any successful fusions. Fresh **peripheral blood lymphocytes** (**PBL**) generate hybrids at a frequency of 1-5/10 power 7 **PBL**'s whereas **PBL**'s cultured for 6 days in the presence of pokeweek mitogen (PWM) prior to fusion yielded at least 4-5 times as many hybrids suggesting preferential fusion with **activated B lymphoblasts**. Hybrids **proliferate** more rapidly and with greater frequency in azaserine/hypoxanthine selection media. These conditions indicate that immortalization of human monoclonal **B cell** populations is feasible using the UC-729-6 cell line and appropriate culture conditions. (0 ref)

L56 ANSWER 87 OF 98 BIOTECHDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 83-09183 BIOTECHDS
TI Human MCA against colon **cancer** produced at Litton; construction of a hybridoma secreting monoclonal

antibody

AU Netzer W J

LO (Pub. Address) Bio/Technology, 15 East 26th St., New York, New York 10010, USA.

SO Bio/Technology; (1983) 1, 7, 537-38

DT Journal

LA English

AN 83-09183 BIOTECHDS

AB A technique for producing human monoclonal **antibodies** against **tumor** antigens associated with human colorectal **cancers** has been developed by Litton Bionetics. Hybridomas are constructed by the fusion of mouse myeloma cells with **peripheral blood lymphocytes** from **cancer** patients who have been immunized against their **tumors**. Potential applications of the technique include **cancer** vaccine production **cancer** diagnostics and therapeutics. The efficiency of Litton hybridoma production is due to an abundant and readily available source of suitable **B cells**. The fact that patients immune responses are directed against antigens common to a variety of colorectal **cancers** is important as regards vaccine preparation. The production of hybridomas producing human **antibody** using **activated B cells** from patients with autoimmune diseases has implications in the study of the pathogenesis and therapy of these diseases. (0 ref)

L56 ANSWER 88 OF 98 CANCERLIT

AN 86622729 CANCERLIT

TI T-CELL GROWTH FACTOR.

AU Robert-Guroff M; Sarngadharan M G; Gallo R C

CS Lab. of Tumor Cell Biology, NCI, NIH, Bethesda, MD

SO Growth Maturation Factors, (1983). Vol. 2, pp. 267-308.

DT Journal; Article; (JOURNAL ARTICLE)

FS ICDB

LA English

EM 8610

AB The factor responsible for the long-term growth of human T-cells in culture, T-cell growth factor (TCGF), has now been purified and its properties analyzed in detail. Since the initial description of human TCGF, studies have proceeded in parallel with TCGF from other species. Although there are some species restrictions, for the most part these factors appear to be analogous to the human TCGF. TCGF is discussed under the following headings: production of TCGF (conditioned media as a source, **activation** of T-cells and production of TCGF, alternate sources of TCGF), purification of TCGF, functions of TCGF (growth of T-cells, induction of cytotoxic T-lymphocytes, regulation of immune interferon production, role in B-lymphocyte differentiation), regulation of TCGF, therapeutic uses of TCGF, TCGF and leukemogenesis, TCGF receptors (direct demonstration of TCGF receptors, correlation between TCGF **binding** and **proliferative** response, affinity and abundance of TCGF receptors), and cloning of TCGF gene. Relatively little is known about the mechanism of action of TCGF or its

regulation, and how these processes may be altered in disease states. (146 Refs)

L56 ANSWER 89 OF 98 CANCERLIT
AN 82922278 CANCERLIT
TI CHARACTERISTICS AND DISTRIBUTION OF ANTIGENS DEFINED BY MONOCLONAL **ANTIBODIES** GENERATED TO COMMON ACUTE LYMPHOBLASTIC LEUKEMIA CELLS.
AU Jones N H
CS Duke University, Durham, NC
SO Diss Abstr Int (Sci), (1982). Vol. 43, No. 3, pp. 674-B.
DT (THESIS)
FS HERN
LA English
EM 8212
AB An attempt was made to produce monoclonal **antibodies** which could be used to subclassify human leukemia cells according to their cell surface phenotype. This report describes the production of a monoclonal **antibody** (DU-ALL-1) to common acute lymphoblastic leukemia (cALL) cells. The cellular and tissue distribution of the DU-ALL-1 antigen and of the 100,000-dalton cALL antigen (CALLA, defined by the J-5 monoclonal **antibody**) was also characterized. Spleen cells from a mouse immunized with cells from patients with cALL were fused with P3 myeloma cells. One hybridoma, DU-ALL-1, reacted only with cALL cell lines and not with lymphoid or myeloid cell lines. **Peripheral blood lymphocytes**, monocytes, granulocytes, and mitogen-**activated** lymphocytes did not react significantly with this **antibody**. However, platelets (100%) and normal bone marrow cells (8%) reacted significantly. Microcytotoxicity testing of human leukemia cells showed that DU-ALL-1 reacted with cells from a majority of null and pre-B ALL patients. Cells from some of these patients reacted only with DU-ALL-1 and not with the J-5 monoclonal **antibody** while cells from other patients gave a reciprocal reactivity. DU-ALL-1 also reacted with cells from a subset of patients with acute myeloblastic leukemia and T-ALL. It was generally non-reactive with cells from patients with **B cell** leukemias and chronic myelogenous leukemias in myeloid blast crisis. By an indirect immunoperoxidase technique, DU-ALL-1 and J-5 reacted with a variety of non-hematopoietic tissues, including kidney, breast, and small intestine. Analysis by sodium dodecyl sulfate-polyacrylamide gel electrophoresis indicated that DU-ALL-1 precipitated an antigen of 24,000 daltons from radioiodinated lysates of cALL cells, platelets, and kidney cells. The DU-ALL-1 antigen did not **bind** to lectins or label metabolically with 3H-glucosamine. J-5 precipitated a molecule from kidney cells which had a lower apparent molecular weight than that precipitated from cALL cells. (no Refs)

L56 ANSWER 90 OF 98 MEDLINE
AN 83061046 MEDLINE
TI Characterization and distribution of a 24,000-molecular weight antigen defined by a monoclonal **antibody** (DU-ALL-1)

elicited to common acute lymphoblastic leukemia (cALL) cells.
AU Jones N H; Borowitz M J; Metzgar R S
NC CA 08975
AM 08054
SO Leuk Res, (1982) 6 (4) 449-64.
Journal code: K9M. ISSN: 0145-2126.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8303
AB A monoclonal **antibody** (DU-ALL-1) was generated to common acute lymphoblastic leukemia (cALL) cells by microcytotoxicity and indirect immunofluorescence, DU-ALL-1 reacted only with cALL cell lines and not with the other hematopoietic cell lines tested. **Peripheral blood lymphocytes**, monocytes, granulocytes and mitogen-**activated** lymphocytes did not react significantly with this **antibody**. However, platelets (100%) and normal bone marrow cells (8.5%) reacted with DU-ALL-1. Microcytotoxicity testing of human leukemia cells showed that DU-ALL-1 reacted with cells from a majority of null and pre-B ALL patients (63/77) and with cells from some patients with acute myeloblastic leukemia (4/7) and T-ALL (4/20). DU-ALL-1 was generally non-reactive with cells from patients with **B-cell** leukemias (2/16) and chronic myelogenous leukemia in blast crisis (0/4). By an indirect immunoperoxidase technique, DU-ALL-1 reacted with a variety of non-hematopoietic tissues, including smooth and cardiac muscle and epithelia from several organs. The DU-ALL-1 antigen had an apparent mol. wt of 24,000 and did not **bind** to lectins or label with [3H]glucosamine. Thus, DU-ALL-1 defines a 24,000-mol. wt protein which is absent from most peripheral blood mononuclear cells, is expressed on normal platelets and several non-hematopoietic tissues, and may be a useful for subclassifying leukemias.

L56 ANSWER 91 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 82089000 EMBASE
TI cAMP receptor proteins and protein kinases in human lymphocytes: fundamental alterations in chronic lymphocytic leukemia cells.
AU Weber W.; Schwoch G.; Wielckens K.; et al.
CS Inst. Physiol. Chem., Univ. Hamburg, Germany, Federal Republic of
SO EUR. J. BIOCHEM., (1981) 120/3 (585-592).
CODEN: EJBCAI
CY Germany, Federal Republic of
LA English
AB To study the significance of cAMP receptor proteins and protein kinase **activities** in **tumor** dys-differentiation, **peripheral blood lymphocytes** from normal donors and from patients with chronic lymphocytic leukemia were isolated by Percoll gradient centrifugation, and analyzed. Both normal and **tumor** lymphocyte populations were devoid of cell **proliferation**. Normal human lymphocytes contained about equal **activities** of histone kinase and 'casein

kinase'. Of the total histone kinase, cAMP-dependent **activity** in normal and **tumor** lymphocytes comprised about 50% as shown by the use of the heat-stable inhibitor. The **tumor** lymphocytes, however, exhibited drastically reduced values of all three protein kinase **activities**, the most pronounced decrease (to 7% of the normal control cells) being observed with the 'casein kinase'. Total high-affinity cAMP-**binding** sites (=regulatory subunits R of cAMP-dependent protein kinases type I and II) in leukemic lymphocytes were also strongly reduced (to < 20%). Immunotitration with specific **antibodies** raised against rabbit muscle RI and bovine heart RII showed that about 60% of the cAMP-**binding** sites were associated with type RI regulatory subunits in both normal and leukemic lymphocytes. Immuno-reactive RII components comprised about 40% of total **binding** sites in lymphocytes of chronic lymphocytic leukemia, but only 20% in normal cells, the residual 20% being represented by RI protein of low immunoreactivity. Combination of gel electrophoretic analysis of the cAMP-**binding** proteins labeled with [32P]n3cAMP and **binding** to the R-specific **antibodies** allowed the identification of individual type I and type II R proteins. Besides the regulatory subunit RI of 49 kDa present in both cell types, additional isoproteins were found, the predominant RII form being a 52 kDa subunit in normal lymphocytes and a 50-kDa subunit in leukemic lymphocytes. The findings in lymphocytes of chronic lymphocytic leukemia cannot be explained by the fact that they are B-type lymphocytes. Control experiments revealed that normal **B cells** do not differ significantly from total blood lymphocytes with respect to the parameters mentioned above. Biochemical correlates of the dys-differentiated status of these non-**proliferating** (G0) cells from patients with chronic lymphocytic leukemia, then, are represented by reduced levels of protein kinases, of basal cAMP, as well as by changes of the R-protein pattern. The data indicate that both protein kinases type I and type II may relate to the state of differentiation, independently from cell **proliferation**.

L56 ANSWER 92 OF 98 LIFESCI COPYRIGHT 1996 CSA
AN 81:38630 LIFESCI
TI Alpha-Fetoprotein on Human **Peripheral Blood Lymphocytes** Does Not Block Complement-Dependent Lymphocytotoxicity.
AU Ren, E.C.; Chan, S.H.
CS WHO Immunol. Res. & Training Ctr., Fac. Med., Univ. Singapore, Singapore 0316
SO SCAND. J. IMMUNOL., (1981) vol. 14, no. 3, pp. 309-313.
DT Journal
FS F
LA English
SL English
AB Using a direct immunofluorescence assay, the authors showed that alpha-fetoprotein (AFP) both in purified form and in hepatocellular **carcinoma** (HCC) sera was capable of **binding** onto

10-20% of T lymphocytes and 5-10% of **B lymphocytes** in human peripheral blood when these lymphocytes were preincubated in AFP positive fluids at 4 degree C in the presence of sodium azide. But when the preincubation temperature was raised to 37 degree C, most of the membrane-**bound** AFP was internalized or shed, and, consequently, less than 3% of the cells showed positive membrane fluorescence. In addition, **binding** of AFP onto lymphocyte surface membrane and the continous presence of large amounts of AFP in these lymphocyte cultures did not interfere with the action of cytotoxic **antibodies** directed against HLA determinants on the lymphocyte surface.

L56 ANSWER 93 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.DUPLICATE 26
AN 79096450 EMBASE
TI Blood lymphocytes in myeloma patients; high percentage of complement receptor bearing cells is accompanied by decreased anti-immunoglobulin (Ig) **binding** capacity.
AU Wetter O.; Linder K.-H.
CS Innere Univ. Klin., Westdeutsches Tumorzent., D-4300 Essen, Germany, Federal Republic of
SO EUR. J. CANCER, (1979) 15/2 (173-182).
CODEN: EJCAAH
CY United Kingdom
LA English
AB Receptor functions of **peripheral blood lymphocytes** of 60 myeloma patients have been studied. Cell surface immunoglobulin, spontaneous rosette formation with SRBC, complement receptors using EAC rosette formation and uptake of radioiodinated **antibodies** against human Ig have been examined and compared to the results obtained with cells from normal individuals. Also the response to polyclonal **B cell activators** has been studied. Significant differences between normal individuals and myeloma patients have been found for the numbers of EAC rosette forming cells. The **binding** capacity for radiolabelled anti-Ig **antibodies** showed a strong tendency to low values in the patient group. Our results are compatible with the idea that cells with an exclusive capacity for complement **binding** are increased in myeloma patients. A high number of EAC **binding** cells has been found also in bone marrow aspirates of myeloma patients showing infiltration by **tumor** cells. Therefore, it seems possible that the site primarily affected from disease is the main source of complement receptor bearing cells. No correlation has been seen between the response to polyclonal **B cell activators** or the concentration of normal serum Ig to the frequency of EAC **binding** cells in individual patients.

L56 ANSWER 94 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 78111093 EMBASE
TI Characterization of cytolytic effector cells in peripheral blood of healthy individuals and **cancer** patients. II. Cytotoxicity

to allogeneic or autochthonous **tumor** cells in tissue culture.

AU Pape G.R.; Troye M.; Perlmann P.

CS Dept. Immunol., Univ. Stockholm, Sweden

SO J.IMMUNOL., (1977) 118/6 (1925-1930).
CODEN: JOIMA3

CY United States

LA English

AB **Peripheral blood lymphocytes** from patients with transitional cell **carcinoma** of the urinary bladder, from control **tumor** patients, and from healthy individuals were fractionated on columns retaining (1) cells with Fc receptors for IgG, as defined by rosette formation with IgG coated erythrocytes, (2) cells with surface **bound** immunoglobulin, or (3) cells with both types of surface markers. The spontaneous cytotoxicity of these lymphocytes against allogeneic or autochthonous **tumor** cells of bladder **carcinoma** or unrelated origin was studied in a 51Cr release assay. The cytotoxicity to allogeneic target cells of lymphocyte fractions depleted of **B cells** (SIg+ cells) was only slightly reduced, unchanged, or, occasionally, augmented when compared to that of unfractionated lymphocytes. Fractions containing the majority of the **B cells** present initially but depleted of most of the Fc receptor bearing lymphocytes (EA+ cells) displayed a strongly reduced cytotoxicity against the same **tumor** cells. These effector cell fractions were also depleted of a majority of the complement receptor bearing lymphocytes (EAC+ cells) and of a minor but significant fraction of T cells (E+ cells) and of a minor but significant fraction of T cells (E+ cells). Removal of both SIg+ and Fc receptor bearing cells gave the same results. Thus, in most instances, the spontaneous cytotoxicity against allogeneic **tumor** cells of fractionated lymphocytes was similar to their K cell **activity** against chicken erythrocytes (Ec) in the presence of rabbit anti Ec **antibodies** (preceding paper). In conjunction with other data on the immunoglobulin dependence of this spontaneous cytotoxicity these results suggest that a significant fraction of this reactivity, displayed by both **tumor** patients' and normal individuals' lymphocytes, may be **antibody** dependent. The **antibodies** may either be carried over cytophilically during lymphocyte isolation or may be formed and released by some **antibody** producing cells during the in vitro incubation. In 2 cases, in which bladder **cancer** patients' lymphocytes were tested with both autochthonous and allogeneic target cells, the effector cells killing the autochthonous target cells were neither **B cells** nor Fc receptor bearing cells. These results suggest that different effector mechanisms were involved in these cases.

L56 ANSWER 95 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.DUPLICATE 27

AN 77085000 EMBASE

TI Effect of radiotherapy on blood lymphocyte population in mammary

carcinoma.
AU Blomgren H.; Berg R.; Wasserman J.; Glas U.
CS Radiumhemmet, Karolinska Sjukh., Stockholm, Sweden
SO INT.J.RADIAT.ONCOL.BIOL.PHYS., (1976) 1/3-4 (177-188).
CODEN: XXXXXB
LA English
AB The **peripheral blood lymphocyte** population in women with primary breast **carcinoma** was studied before and after local radiotherapy. It was found that local radiotherapy, given pre or postoperatively, reduces the number of peripheral lymphocytes by approximately 50%. The frequency of lymphocytes having membrane associated receptors for **activated** complement (mainly **B cells**) was significantly decreased after radiotherapy whilst cells **binding** sheep erythrocytes to their cell membrane (T cell) increased. The relative responsiveness of the lymphocytes to purified protein of tuberculin (PPD) in vitro was significantly reduced after irradiation. On the other hand, the response of the cell to the nonspecific mitogens phytohaemagglutinin (PHA) or poke weed mitogen (PWM) remained unchanged. The capacity of the patients to maintain their natural serum **antibody** levels against herpes simplex, Cytomegalo virus, or Morbilli was unaffected.

L56 ANSWER 96 OF 98 CANCERLIT
AN 77702857 CANCERLIT
TI DETERMINATION OF THE ORIGIN OF MALIGNANT RETICULAR CELLS BY THE USE OF SURFACE MEMBRANE MARKERS.
AU Green I; Jaffe E S; Shevach E M; Edelson R L; Frank M M; Berard C W
SO Non-serial, (1975). International Academy of Pathology Monograph. Rebuck JW, Berard CW, Abell MR, ed. Baltimore, Williams and Wilkins Co, 1975.
DT Book; (MONOGRAPH)
FS CARC
LA English
EM 7704
AB A number of **neoplastic** lymphoreticular **proliferations** were investigated for the presence of the IgM EAC (erythrocytes coated with **antibody** and complement), IgG EA (erythrocytes coated with **antibody**), and E receptors to determine if the presence or absence of these various receptors would permit classification of cellular elements as to their origin from **B cells**, T cells, or histiocytes. **Neoplastic** cells from a case of histiocytic medullary reticulosis and from two cases of leukemic reticuloendotheliosis demonstrated only one of the receptors of normal peripheral blood histiocytes, that for IgG EA. These **neoplastic** cells demonstrated a receptor for cytophilic **antibody** characteristic of histiocytes or monocytes, and failed to demonstrate any markers of either B or T lymphocytes. Cells from a case of nodular or follicular lymphoma **bound** IgM EAC but failed to **bind** IgG EA or E. These **binding** properties are characteristic of **B cells** of the normal lymphoid follicle. In three cases of

diffuse lymphocytic lymphoma, the **neoplastic** cells formed E rosettes, and by this criterion they were T lymphocytes. A high percentage of the cells from eight patients with chronic lymphocytic leukemia (CLL) had receptors for IgM EAC. This fact plus the observation that the lymphocytes of most CLL patients have immunoglobulins of a single class on their surface as well as the Fc receptor strongly indicate that CLL is a monoclonal malignancy of the **B cell** system. A high percentage of the **peripheral blood lymphocytes** of three patients with chronic leukemia and erythroderma, who had the Sezary syndrome, formed E rosettes. **B cell** markers, the presence of surface immunoglobulin, and the ability to form rosettes with EgM EAC were absent on these lymphocytes. These and other results indicate that the abnormal cell of the Sezary syndrome is a T cell. By these same techniques, the abnormal cells infiltrating the plaques of three patients with mycosis fungoides were also T cells, indicating a close relationship between these two diseases. Eventually, this research will lead to a new classification of reticuloendothelial **neoplasms** that will be of greater diagnostic and prognostic value. (46 refs)

L56 ANSWER 97 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 75201604 EMBASE
TI Characterization of human **B lymphocyte** specific antigens.
AU Ishii Y.; Koshiba H.; Ueno H.; et al.
CS Dept. Pathol., Sapporo Med. Coll., Saporo, Japan
SO J.IMMUNOL., (1975) 114/1(II) (466-469).
CODEN: JOIMA3
LA English
AB Antihuman **B cell** serum (ABS) was developed by sequentially absorbing a rabbit antihuman tonsil serum (AHTS) with human red cells, liver, serum, and thymocytes. AHTS was also absorbed quantitatively with tissues and cells from different sources. ABS was nontoxic for thymocytes but lysed the majority of chronic lymphocytic leukemia (CLL) cells. This also killed a number of tonsil and blood lymphocytes which **bound** erythrocyte **antibody** complement complexes but not sheep erythrocytes. In further studies, it was shown that phytohemagglutin responsibility of **peripheral blood lymphocytes** was not affected by treating them with ABS and complement. AntiB cell **activity** of AHTS was not changed by absorption with thymus, liver, kidney, and brain tissues but absorbed with tonsil and CLL cells. These data confirm the **B cell** specificity of ABS. Indirect immunofluorescence was carried out on tissue sections of human tonsils and lymph nodes, which indicated that ABS reactive cells were concentrated in lymphoid follicles including germinal centers, while plasma cells and cells located in the thymus dependent area were essentially devoid of immunofluorescence.

L56 ANSWER 98 OF 98 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 75069503 EMBASE
TI Lymphocyte subpopulations in chronic lymphocytic leukemia.

Characterization by cell surface markers, cytotoxic **activity**
, and mitogenic stimulation.
AU Mellstedt H.; Pettersson D.
CS Dept. Med., Seraphimer Hosp., Stockholm, Sweden
SO SCAND.J.IMMUNOL., (1974) 3/3 (303-310).
CODEN: SJIMAX
LA English
AB **Peripheral blood lymphocytes** from 8
patients with chronic lymphocytic leukemia (CLL) were studied.
Characterization by different cell surface markers showed low
percentages of lymphocytes that **bound** sheep erythrocytes
and had receptors for **activated** human complement but
markedly increased numbers of cells that carried surface
immunoglobulins. It is concluded that Ig bearing lymphocytes are
mainly responsible for the lymphocytosis in CLL. The capacity of CLL
lymphocytes to lyse 51Cr labeled chicken erythrocytes in vitro in
the presence of phytohemagglutinin (PHA) or **antibodies**
against target cells was reduced. A strong correlation was found
between the percentages of complement receptor bearing lymphocytes
and their **antibody** induced cytotoxicity. The ability of
CLL lymphocytes to synthetize DNA after stimulation with PHA or
pokeweed mitogen (PWM) was reduced. The impairment of stimulation
was more pronounced at low concentrations of PWM than at high
concentrations. This observation is in line with the assumption that
low doses of PWM **activate** mainly bone marrow derived
lymphocytes and that the normal **B lymphocyte**
population is replaced by leukemic cells in CLL.

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E5	8		KUHAJDA FRANCIS P/AU
E6	7		KUHAJDA K/AU
E7	12		KUHAJDA KSENIJA/AU
E8	1		KUHAJDA KSENIJA MARIA/AU
E9	2		KUHAJEK E J/AU
E10	9		KUHAJEK EUGENE J/AU

_Author (S)

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             8 "KUHAJDA FRANCIS P"/AU
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E2           1      PASTERNACK ERIC STEPHEN/AU
E3           3 --> PASTERNACK G/AU
E4           1      PASTERNACK GARY/AU
E5          19      PASTERNACK GARY R/AU
E6          23      PASTERNACK GEORGE/AU
E7           1      PASTERNACK GREGORY B/AU
E8           1      PASTERNACK JACYR/AU
E9           4      PASTERNACK JENNIFER M/AU
E10         16      PASTERNACK L/AU

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?carcin? or ?tumor? or ?tumour?)
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             1 "PASTERNACK GARY"/AU
            19 "PASTERNACK GARY R"/AU
L58         23 ("PASTERNACK G"/AU OR "PASTERNACK GARY"/AU OR "PASTERNACK
               GARY R"/AU)


L59          4 L57 AND L58


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        184127 ?NEOPLAS?
        100413 ?CARCIN?
        167130 ?TUMOR?
           258 ?TUMOUR?
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        101712 ?CARCIN?
        169713 ?TUMOR?
           265 ?TUMOUR?
L62          16 L59 OR L60

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L63  ANSWER 1 OF 16  CA  COPYRIGHT 1996 ACS              DUPLICATE 1
AN   122:211535  CA
TI   Simplified high-sensitivity sequencing of a major histocompatibility
     complex class I-associated immunoreactive peptide using
     matrix-assisted laser desorption/ionization mass spectrometry
SO   Anal. Biochem. (1995), 226(1), 15-25
     CODEN: ANBCA2; ISSN: 0003-2697
AU   Woods, Amina S.; Huang, Alex Y. C.; Cotter, Robert J.;
   Pasternack, Gary R.; Pardoll, Drew M.; Jaffee, Elizabeth M.
PY   1995
AB   Cytotoxic T cells (CTL) are known to recognize small peptide
     fragments of cytoplasmic proteins bound to major histocompatibility
     complex (MHC) class I mols. on cell surfaces.  Recent work indicates
     that tumor antigens are processed and presented in a
     manner similar to viral antigens.  Identification of the peptides
     recognized by tumor-specific CTL would provide valuable
     information about their parent proteins, as well as allowing for the
     development of recombinant antigen-specific tumor
     vaccines.  While highly represented MHC-bound peptides have been
     routinely purified by reversed-phase HPLC for Edman degrdn.
     sequencing, identification and sequencing of infrequent peptides
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that represent the biol. relevant targets of **tumor** -specific CTL have proved elusive. We have combined matrix-assisted laser desorption/ionization mass spectrometry with on-slide exopeptidase digestion to successfully identify and directly sequence a model **tumor**-specific peptide antigen derived from an integrated viral gene. The enhanced sensitivity of this technique (femtomolar range) allows for the sequencing of specific MHC-bound peptides derived from as few as 1 .times. 109 cells.

L63 ANSWER 2 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 2
AN 121:26885 CA
TI Chemotherapy of **cancer** by inhibition of fatty acid synthetase
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
IN **Kuhajda, Francis P.; Pasternack, Gary R.**
AI WO 93-US7023 930726
PI WO 9402108 A1 940203
PY 1994
AB Fatty acid synthase (FAS) is at very high levels in **carcinomas** with poor prognosis, but little FAS activity is found in normal tissues. Inhibition of fatty acid synthesis is selectively toxic to **carcinoma** cells, while normal cells with low FAS activity are resistant. This invention provides a method of treating **cancer** patients where fatty acid synthesis by cells of the patient's **tumor** is inhibited with resultant interruption of the disease process. A protein OA-519 was found to be a prognostic marker of breast and ovarian **cancer** and prostatic **adenocarcinoma** using immunohistochem. detn. of protein levels. The protein was purified from ZR-75-1 cells by chromatog. on Sephacryl S-200, anion-exchange HPLC and chromatog. on hydroxyapatite. The protein was shown to be able to incorporate 14C-malonyl-CoA into fatty acids. The fatty acid synthase inhibitors cerulenin and melarsoprol inhibited the growth of the breast **cancer** cell line ZR-75-1 but had no effect on normal fibroblasts; the inhibition could be reversed by high exogenous levels of oleate. Hybridization assays indicated that high levels of OA-519 were due to increased transcription but not gene amplification. Inhibitors of other activities essential in lipid synthesis, e.g. acetyl-CoA carboxylase were also effective against cell lines with high levels of OA-519.

L63 ANSWER 3 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 3
AN 121:73281 CA
TI Fatty acid synthesis: a potential selective target for **antineoplastic** therapy
SO Proc. Natl. Acad. Sci. U. S. A. (1994), 91(14), 6379-83
CODEN: PNASA6; ISSN: 0027-8424
AU **Kuhajda, Francis P.**; Jenner, Kris; Wood, Fawn D.; Hennigar, Randolph A.; Jacobs, Lisa B.; Dick, James D.; **Pasternack, Gary R.**
PY 1994
AB OA-519 is a prognostic mol. found in **tumor** cells from

breast **cancer** patients with markedly worsened prognosis. The authors purified OA-519 from human breast **carcinoma** cells, obtd. its peptide sequence, and unambiguously identified it as fatty acid synthase through sequence homol. and enzymol. **Tumor** fatty acid synthase is an .apprxeq.270-kDa polypeptide which specifically abolished immunostaining of human breast **cancers** by anti-OA-519 antibodies. **Tumor** fatty acid synthase oxidized NADPH in a malonyl-CoA-dependent fashion and synthesized fatty acids composed of 80% palmitate, 10% myristate, and 10% stearate from acetyl-CoA, malonyl-CoA, and NADPH with a specific activity of 624 nmol of NADPH oxidized per min per mg. **Tumor** cell lines with elevated fatty acid synthase showed commensurate increases in incorporation of [U-14C]acetate into acylglycerols, demonstrating that fatty acid synthase increases occur in the context of overall increases in endogenous fatty acid synthesis. Cerulenin inhibited acylglycerol synthesis in **tumor** cells and fibroblast controls in a dose-dependent fashion and also caused a growth inhibition which generally paralleled the level of endogenous fatty acid synthesis. Supraphysiol. levels of palmitate, 14 .mu.M in DMSO, significantly reversed the growth inhibition caused by cerulenin at concns. of .ltoreq.5 .mu.g/mL, indicating that cerulenin-mediated growth inhibition was due to fatty acid synthase inhibition.

L63 ANSWER 4 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 4
AN 120:294762 CA
TI Identification of human acetyl-CoA carboxylase isoenzymes in tissue and in breast **cancer** cells
SO Int. J. Biochem. (1994), 26(4), 589-94
CODEN: IJBOBV; ISSN: 0020-711X
AU Witters, Lee A.; Widmer, Jane; King, Aimee Nicole; Fassihi, Kathy; **Kuhajda, Francis**
PY 1994
AB In the rat, acetyl-CoA carboxylase (ACC), a rate-limiting enzyme in fatty acid metab., exists as at least two different isoenzymes (Mr 265,000 and 280,000) that display distinct tissue-specific distribution and regulation. Based on the study of human tissue and human-derived breast **cancer** cell lines by enzyme isolation and protein blotting techniques, the authors have now identified two human isoforms of Mr 265,000 (HACC 265) and 275,000 (HACC 275), each of which is homologous to one of the rat isoenzymes. Human breast **carcinoma** cell lines show variable expression of these two isoforms, mirrored in the estn. of ACC acetyl-CoA kinetics.

L63 ANSWER 5 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 5
AN 120:28404 CA
TI A novel Mr 32,000 nuclear phosphoprotein is selectively expressed in cells competent for self-renewal
SO Cancer Res. (1993), 53(19), 4720-6
CODEN: CNREA8; ISSN: 0008-5472
AU Walensky, Loren D.; Coffey, Donald S.; Chen, Tseng Hui; Wu, Tzyy Choou; **Pasternack, Gary R.**
PY 1993

AB The authors investigated the assocn. between expression of a novel Mr 32,000 nuclear phosphoprotein (pp32) and cell proliferation in vivo using the well characterized physiol. model of androgen-dependent regeneration of prostate in orchiectomized rats. Pp32 is expressed at high levels in **neoplastic** cell lines and in certain anatomically defined stem cell compartments of normal human tissues such as intestinal crypt epithelial cells. Immunohistochem. and in situ hybridization were used to monitor pp32 expression in rat ventral prostatic epithelium following castration and androgen restoration. Castrated rats retained only 6% of prostate wet wt. compared to intact controls but were capable of complete gland restoration upon androgen replacement. In intact controls, pp32 expression localized to small acini at the periphery of the gland and to rare basal cells in the central regions. Ten days following castration, there was a 3.5-fold enrichment in the frequency of pp32-pos. cells with greater than 56% of remaining epithelial cells expressing pp32 protein. In situ hybridization showed that all remaining epithelial cells contained pp32 mRNA. Upon testosterone replacement, pp32 expression and localization returned to that of intact controls. In order to det. the assocn. between pp32 expression and cell division, DNA synthesis was monitored by bromodeoxyuridine incorporation during prostate involution and regeneration. Bromodeoxyuridine incorporation peaked 3 days after androgen replacement and occurred diffusely throughout the gland. Thus, pp32-pos. cells are anatomically distinguishable from the population of terminally differentiating cells undergoing rapid expansion. Preliminary immunohistochem. studies of human prostatic **neoplasia** demonstrated increased expression of pp32 in human prostatic **adenocarcinoma** and prostatic intraepithelial **neoplasia** compared to benign prostatic hypertrophy and normal human prostate. The highest degree of expression occurred in the higher Gleason grades and prostatic intraepithelial **neoplasia**. This work suggests that pp32 is a nuclear protein which has a selective but presently undefined role in cells competent for self-renewal.

L63 ANSWER 6 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 6
AN 116:251684 CA
TI Nuclear phosphoproteins for prognosticating lymphoid or epithelial **cancers**
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
IN **Pasternack, Gary R.**
AI WO 91-US5452 910801
PI WO 9202554 A1 920220
PY 1992
AB Nuclear phosphoproteins pp32, pp35, pp42 (32, 35, and 42 kDa, resp.) are disclosed which are useful in the diagnosis and prognosis of **tumors** of lymphoid and epithelial origin. The 3 proteins are immunol. related to each other. The level of expression of the proteins correlates with the malignant potential of lymphoid and epithelial **tumors**. In addn., in some cases the subcellular location of the proteins is indicative of malignant

potential. Antibodies reactive with the proteins are disclosed as diagnostic tools, nucleic acid probes and primers for quantitating the mRNAs encoding the proteins. Methods for prepg. and purifying the proteins are also taught. A portion of the cDNA sequence and derived amino acid sequence for pp35 of murine cell line A20 is shown.

L63 ANSWER 7 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 7
AN 114:97805 CA
TI Preparation of haptoglobin-related (Hpr) proteins and its application in diagnosis of **cancer**
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
IN **Kuhajda, Francis P.; Pasternack, Gary R.**
AI WO 90-US26 900105
PI WO 9008324 A1 900726
PY 1990
AB Substantially pure prepns. of Hpr protein are prepd. from, e.g., human breast **cancer** cells, dicidua cells, or placental tissue by testing a cell line for the ability to bind to antibodies which are immunoreactive with epitopes found on Hpr protein but not found on haptoglobin 1 or 2, culturing reactive cell lines, and harvesting Hpr protein from the cytoplasmic fraction. The antigen for raising anti-Hpr protein antibodies is a peptide comprising the 34 N-terminal amino acids of the .alpha.-chain of the Hpr protein conjugated to keyhole limpet hemocyanin. The Hpr protein has use as diagnostic marker correlated with early relapse and metastasis of human breast and other **cancers**. Immunoassay methods and kits using the antibodies are given. Thus, Hpr protein was first isolated from human pregnancy plasma and purified by successive chromatog. on Cibacron Blue F3G-A Sepharase, DE-52 DEAE-cellulose, Fast Flow Q-Sepharose CL-4B, and final purifn. by HPLC on a Mono Q HR5/5 column. The product was screened by immunoreaction with anti-Hpr antibody. Anti-Hpr protein antibody was raised by immunization of rabbits with the 34-mer synthetic Hpr peptide conjugate and used to detect Hpr protein by immunohistochem. staining a primary breast **adenocarcinoma** in the presence of anti-**carcinoembryonic** antigen antibody.

L63 ANSWER 8 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 8
AN 113:93588 CA
TI Identification and preliminary characterization of two related proliferation-associated nuclear phosphoproteins
SO J. Biol. Chem. (1990), 265(22), 13400-9
CODEN: JBCHA3; ISSN: 0021-9258
AU Malek, Sami N.; Katumuluwa, Asoka I.; **Pasternack, Gary R.**
PY 1990
AB Two nuclear phosphoproteins, pp35 and pp32, were purified from A20 cells, a murine B-lymphoblastoid cell line. Initially detected by cross-reactivity with antibodies to human erythrocyte protein 4.1, the 35- and 32-kDa proteins were purified by sequential fractionation of nonionic detergent cell lysates on DEAE-cellulose, HPLC-anion-exchange chromatog., and HPLC hydroxylapatite chromatog.

By two-dimensional peptide mapping, pp35 and pp32 are related but do not appear to represent sequential proteolytic products. Both pp35 and pp32 appear to be assocd. with cell proliferation. Antibodies specific for pp35 and pp32 show prominent intranuclear staining in A20 cells but only focal staining in normal murine lymphoid tissues. Quant. immunoblotting showed that both pp35 and pp32 are, resp., expressed at 5.9 .times. 104 and 7.0 .times. 104 copies/cell in small, dense resting B lymphocytes, increasing .apprx.12- and 7-fold after polyclonal stimulation with lipopolysaccharide. When normalized to total cell protein, this represents specific inductions of .apprx.4- and 2-fold. Expression of both pp35 and pp32 is constitutively high in populations of **neoplastic** B cell lines; moreover, both are expressed in the nuclei of intestinal crypt epithelial cells but not in other epithelial compartments in the same sections, suggesting that forms of pp35 and pp32 may be expressed in addnl. tissues and assocd. with proliferation.

L63 ANSWER 9 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 9
AN 110:133261 CA
TI Expression of haptoglobin-related protein and its potential role as a **tumor** antigen
SO Proc. Natl. Acad. Sci. U. S. A. (1989), 86(4), 1188-92
CODEN: PNASA6; ISSN: 0027-8424
AU **Kuhajda, Francis P.**; Katumuluwa, Asoka I.; **Pasternack, Gary R.**
PY 1989
AB The detection of a haptoglobin species, its characterization as the HPR gene product, and its assocn. with both pregnancy and **neoplasia** are described. Previous work showed that the early recurrence of human breast **cancer** correlated with immunohistochem. staining with a com. antiserum directed against pregnancy-assocd. plasma protein A (PAPP-A). Use of this antiserum to guide purifn. of the putative antigen led to the present identification and purifn. of a strongly immunoreactive protein species distinct from PAPP-A that was present in the plasma of pregnant women at term. This immunoreactive protein consists of a light (.alpha.) chain (16.5 kDa) and a heavy (.beta.) chain (40 kDa); protein microsequencing of the .beta. chain showed it to be a member of the haptoglobin family. The .alpha. chain of this haptoglobin species differs from ordinary haptoglobin 1 and 2 .alpha. chains both structurally and immunol. and represents the product of the HPR gene, haptoglobin-related protein (Hpr), since (i) the apparent mol. mass is the same as that predicted for Hpr .alpha. chain, (ii) the peptide map differs from that of haptoglobin 1 in a manner predicted by the HPR nucleotide sequence, (iii) monospecific antibodies that react with epitopes shared by the unique .alpha. chain and a synthetic peptide derived from the HPR nucleotide sequence do not detect these epitopes in either haptoglobin 1 or 2, and (iv) sequences of .alpha.-chain peptides were consistent with this identification, excluding haptoglobin 1 but not haptoglobin 2. Staining of **neoplastic** breast tissue is abolished by preincubation with purified Hpr.

L63 ANSWER 10 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 10
AN 105:131453 CA
TI Merkel cell (small cell) **carcinoma** of the skin: immunohistochemical and ultrastructural demonstration of distinctive perinuclear cytokeratin aggregates and a possible association with B cell **neoplasms**
SO Histochem. J. (1986), 18(5), 239-44
CODEN: HISJAE; ISSN: 0018-2214
AU **Kuhajda, Francis P.**; Olson, Jean L.; Mann, Risa B.
PY 1986
AB The immunohistochem. of epithelial and neuroendocrine antigens in 3 cases of Merkel cell (small cell) **carcinoma** of the skin is presented. All 3 cases showed distinctive punctate perinuclear cytoplasmic positivity for cytokeratin which corresponded to aggregates of intermediate filaments, seen ultrastructurally in 2 cases. Epithelial membrane antigen was also identified in 2 cases. Only 1 case showed cytoplasmic positivity for neuron-specific enolase, and immunostaining for a battery of polypeptide hormones was neg. The demonstration of cytokeratin perinuclear inclusions provides a distinctive immunohistochem. feature to aid in their diagnosis. Two of the 3 patients had chronic lymphocytic leukemia years before the diagnosis of Merkel cell **carcinoma**. The possible assocn. of lymphoproliferative disorders, particularly B cell **tumors**, and Merkel cell **carcinoma** is discussed.

L63 ANSWER 11 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 11
AN 89:22152 CA
TI **Tumor** cell cytostasis by macrophages and antibody in vitro. II. Isolation and characterization of suppressed cells
SO J. Immunol. (1978), 120(5), 1567-72
CODEN: JOIMA3; ISSN: 0022-1767
AU **Pasternack, Gary R.**; Johnson, Robert J.; Shin, Hyun S.
PY 1978
AB **Tumor** cells in a cytostatic state caused by macrophages and antibody were isolated. Such suppressed cells excluded vital dye, incorporated uridine and leucine, and metabolized glucose. They did not, however, incorporate thymidine, nor did they resume cell division in culture. During prolonged culture, these cells eventually died. In this system, cytostasis was an all-or-nothing phenomenon at the level of the individual cell. Once in the cytostatic state **tumor** cells did not resume proliferation.

L63 ANSWER 12 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 12
AN 89:22151 CA
TI **Tumor** cell cytostasis by macrophages and antibody in vitro. I. Resolution into contact-dependent and contact-independent steps
SO J. Immunol. (1978), 120(5), 1560-6
CODEN: JOIMA3; ISSN: 0022-1767
AU **Pasternack, Gary R.**; Johnson, Robert J.; Shin, Hyun S.
PY 1978
AB In a murine system, macrophages, in concert with antibody,

suppressed iododeoxyuridine incorporation by **tumor** cells. The mechanism of suppression did not involve phagocytosis or lysis. The generation of suppressed **tumor** cells was resolved into a contact-dependent step and a contact-independent step. The first step was one-hit with respect to macrophages and multi-hit with respect to antibody.

L63 ANSWER 13 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 13
AN 89:177723 CA
TI Mechanisms of **tumor** immunity: the role of antibody and nonimmune effectors
SO Prog. Allergy (1978), 25, 163-210
CODEN: PRALAD; ISSN: 0079-6034
AU Shin, Hyun S.; Johnson, Robert J.; **Pasternack, Gary R.**; Economou, James S.
PY 1978
AB A review with 286 refs. of mobilization, activation, and suppressive activity of nonimmune effectors in suppression of **tumor** growth and the regulatory effects of antibody upon active **tumor** immunity. Practical applications are discussed.

L63 ANSWER 14 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 14
AN 86:137601 CA
TI Antibody-mediated suppression of **tumor** growth. III. Molecular assay of murine IgG1 alloantibody required to cause **tumor** suppression in vivo
SO J. Immunol. (1977), 118(2), 498-504
CODEN: JOIMA3
AU Johnson, Robert J.; **Pasternack, Gary R.**; Drysdale, B. E.; Shin, Hyun S.
PY 1977
AB A radioimmunoassay was used to quantitate the no. of **tumor** cell-bound IgG1 **antitumor** antibody mols. required to cause suppression of **tumor** growth in C3H mice. Radiolabeled anti-IgG1 was used to detect cell-bound IgG1 antibody. The assay was calibrated by using TNP-coupled **tumor** cells that had a known no. of bound IgG1 anti-deoxyribonucleoprotein mols. IgG1 **antitumor** antibody at 70,000-130,000 mols./**tumor** cell were sufficient to cause 50% suppression of **tumor** growth in mice inoculated with .apprx.50,000 **tumor** cells.

L63 ANSWER 15 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 15
AN 86:137600 CA
TI Antibody-mediated suppression of **tumor** growth. II. Macrophage and platelet cooperation with murine IgG1 isolated from alloantiserum
SO J. Immunol. (1977), 118(2), 494-7
CODEN: JOIMA3
AU Johnson, Robert J.; **Pasternack, Gary R.**; Shin, Hyun S.
PY 1977
AB The effectors that cooperated with IgG1 antibodies in causing **tumor** suppression were identified as exudate macrophages and blood platelets in animals syngeneic and allogeneic to the

tumor. Lymphocytes were not active in suppressing **tumor** growth in the presence of IgG1 antibody, although they were active in whole antiserum.

L63 ANSWER 16 OF 16 CA COPYRIGHT 1996 ACS DUPLICATE 16
AN 86:137599 CA
TI Antibody-mediated suppression of **tumor** growth. I. Suppression by murine IgG1 isolated from alloantiserum
SO J. Immunol. (1977), 118(2), 489-93
CODEN: JOIMA3
AU Johnson, Robert J.; **Pasternack, Gary R.**; Shin, Hyun S.
PY 1977
AB The **tumor** suppressive activity in murine IgG1 antibody was studied in vivo. IgG1 was isolated from hyperimmune alloantisera against a murine lymphoma, 6C3HED, by absorption with heat-killed, formalinized Staphylococcus aureus Cowan strain I, followed by DEAE ion exchange chromatog. and Sephadex G-200 gel filtration chromatog. The isolated IgG1, which had no detectable IgM, IgA, IgG2a, IgG2b, or IgG3, could suppress the growth of the **tumor**. In addn., DEAE and Sephadex G-200 column profiles of the in vivo **tumor** suppressive activity showed good correlation with the profiles of total IgG1 immunoglobulin and anti-**tumor** antibody assayed for IgG1 heavy chains and .kappa. light chains. The IgG1 **tumor** suppressive activity was not diminished after heating at 56.degree. for 30 min.

FILE 'BIOSIS' ENTERED AT 16:37:15 ON 24 JAN 96
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 12 January 1996 (960112/ED)
CAS REGISTRY NUMBERS (R) LAST ADDED: 12 January 1996 (960112/UP)

L64 85 KUHAJDA F?/AU

L65 59 PASTERNACK G?/AU

=> l64 and l65; s (l64 or l65) and (cancer? or neoplas? or carcin? or tum? or antitum? or anticancer? or anticarcin? or antineoplas?)
'L64' IS NOT A RECOGNIZED COMMAND
COMMAND STACK INTERRUPTED. ENTER "DISPLAY HISTORY" TO SEE WHICH COMMANDS WERE EXECUTED.

The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

```
=> s l64 and l65; s (l64 or l65) and (cancer? or neoplas? or carcin? or
tum? or antitum? or anticancer? or anticarcin? or antineoplas?)
L66          20 L64 AND L65


         234398 CANCER?
          82522 NEOPLAS?
         285448 CARCIN?
         360338 TUM?
          20935 ANTITUM?
           6243 ANTICANCER?
           1224 ANTICARCIN?
         140912 ANTINEOPLAS?
L67          80 (L64 OR L65) AND (CANCER? OR NEOPLAS? OR CARCIN? OR TUM? O
                R ANTITUM? OR ANTICANCER? OR ANTICARCIN? OR ANTINEOPLAS?)

=> s l66 and (cancer? or neoplas? or carcin? or tum? or antitum? or
anticancer? or anticarcin? or antineoplas?)
         234398 CANCER?
          82522 NEOPLAS?
         285448 CARCIN?
         360338 TUM?
          20935 ANTITUM?
           6243 ANTICANCER?
           1224 ANTICARCIN?
         140912 ANTINEOPLAS?
L68          19 L66 AND (CANCER? OR NEOPLAS? OR CARCIN? OR TUM? OR ANTITUM
                ? OR ANTICANCER? OR ANTICARCIN? OR ANTINEOPLAS?)

=> s (l67 or l68) and antibod?
         354187 ANTIBOD?
L69          21 (L67 OR L68) AND ANTIBOD?

=> s l69 not l55; fil medl; s l64; s l65
L70          21 L69 NOT L55


FILE 'MEDLINE' ENTERED AT 16:40:54 ON 24 JAN 96

 FILE LAST UPDATED: 27 DEC 1995 (951227/UP).  FILE COVERS 1966 TO DATE.
 +QLF/CT SHOWS YOU THE ALLOWABLE QUALIFIERS OF A TERM.

 MEDLINE, CANCERLIT AND PDQ ERRONEOUSLY ANNOTATED CERTAIN ARTICLES
 AUTHORED OR CO-AUTHORED BY DR. BERNARD FISHER WITH THE PHRASE
 "SCIENTIFIC MISCONDUCT-DATA TO BE REANALYZED."  ALL SUCH ANNOTATIONS
 HAVE BEEN REMOVED OR ARE BEING REMOVED.  WE APOLOGIZE FOR ANY PROBLEMS
 OR CONCERNS THIS MAY HAVE CAUSED.  USERS SHOULD DISREGARD THOSE PRIOR
 ANNOTATIONS.


L71          57 KUHAJDA F?/AU
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L72          27 PASTERNACK G?/AU

=> s l71 and l72; s l71 or l72
L73           5 L71 AND L72


L74          79 L71 OR L72

=> s (l73 or l74) and (cancer? or neoplas? or carcin? or tum? or antitum?
or anticancer? or anticarcin? or antineoplas?)
        220938 CANCER?
        799959 NEOPLAS?
        269796 CARCIN?
        388923 TUM?
         19608 ANTITUM?
          5927 ANTICANCER?
          1291 ANTICARCIN?
         79034 ANTINEOPLAS?
L75          55 (L73 OR L74) AND (CANCER? OR NEOPLAS? OR CARCIN? OR TUM? O
               R ANTITUM? OR ANTICANCER? OR ANTICARCIN? OR ANTINEOPLAS?)

=> s l75 and antibod?
        426022 ANTIBOD?
L76          19 L75 AND ANTIBOD?

=> s l76 not l34; fil biotechds; s l76
L77          19 L76 NOT L34


FILE 'BIOTECHDS' ENTERED AT 16:43:31 ON 24 JAN 96
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             0 KUHAJDA F?/AU
             0 PASTERNACK G?/AU
             0 KUHAJDA F?/AU
             0 PASTERNACK G?/AU
          3559 CANCER?
           409 NEOPLAS?
          2657 CARCIN?
         10224 TUM?
          2694 ANTITUM?
           123 ANTICANCER?
            13 ANTICARCIN?
            79 ANTINEOPLAS?
         19924 ANTIBOD?
L78           0 L75 AND ANTIBOD?

=> fil embas; s l76; fil lifesci; s l76; fil cancerlit; s l76; fil wpids;
s l76
```

FILE 'EMBASE' ENTERED AT 16:44:06 ON 24 JAN 96

FILE COVERS 1974 TO 16 Jan 1996 (960116/ED)

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            49 KUHAJDA F?/AU
            28 PASTERNACK G?/AU
            49 KUHAJDA F?/AU
            28 PASTERNACK G?/AU
        409388 CANCER?
        396383 NEOPLAS?
        253567 CARCIN?
        393580 TUM?
         17710 ANTITUM?
          5929 ANTICANCER?
           775 ANTICARCIN?
         31140 ANTINEOPLAS?
        307860 ANTIBOD?
L79          17 L75 AND ANTIBOD?
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FILE 'LIFESCI' ENTERED AT 16:44:54 ON 24 JAN 96

FILE COVERS 1978 TO 19 Jan 1996 (960119/ED)

```
            11 KUHAJDA F?/AU
             6 PASTERNACK G?/AU
            11 KUHAJDA F?/AU
             6 PASTERNACK G?/AU
         19665 CANCER?
          7356 NEOPLAS?
         29051 CARCIN?
         46965 TUM?
          5300 ANTITUM?
           842 ANTICANCER?
           162 ANTICARCIN?
          3206 ANTINEOPLAS?
        104615 ANTIBOD?
L80           3 L75 AND ANTIBOD?
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FILE 'CANCERLIT' ENTERED AT 16:45:05 ON 24 JAN 96

FILE COVERS 1963 TO 5 Dec 1995 (951205/ED)

MEDLINE, CANCERLIT, and PDQ erroneously annotated certain articles authored or co-authored by Dr. Bernard Fisher with the phrase "scientific misconduct-data to be reanalyzed." All such annotations have been removed or are being removed. We apologize for any problems

or concerns that this may have caused. Users should disregard those prior annotations.

Cancerlit has been reloaded with 1995 MeSH headings. See NEWS FILE and HELP RLOAD for details.

```
            48 KUHAJDA F?/AU
            20 PASTERNACK G?/AU
            48 KUHAJDA F?/AU
            20 PASTERNACK G?/AU
        245284 CANCER?
        546558 NEOPLAS?
        263995 CARCIN?
        429832 TUM?
         26947 ANTITUM?
          7974 ANTICANCER?
          1623 ANTICARCIN?
         76139 ANTINEOPLAS?
        101365 ANTIBOD?
L81         20 L75 AND ANTIBOD?


FILE 'WPIDS' ENTERED AT 16:48:03 ON 24 JAN 96
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FILE LAST UPDATED: 22 JAN 96                <960122/UP>
>>>UPDATE WEEKS:
MOST RECENT DERWENT WEEK             9603   <199603/DW>
DERWENT WEEK FOR CHEMICAL CODING:    9543
DERWENT WEEK FOR POLYMER INDEXING:   9550
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
>>> DERWENT POLYMER INDEXING THESAURUS AVAILABLE IN FIELD /PLE <<<
     >>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<


             3 KUHAJDA F?/AU
            13 PASTERNACK G?/AU
             3 KUHAJDA F?/AU
            13 PASTERNACK G?/AU
         11767 CANCER?
          2139 NEOPLAS?
          5592 CARCIN?
         19381 TUM?
          6882 ANTITUM?
          2651 ANTICANCER?
           149 ANTICARCIN?
           860 ANTINEOPLAS?
         20683 ANTIBOD?
L82          1 L75 AND ANTIBOD?

=> dup rem l70,l77,l79,l80,l81,l82
FILE 'WPIDS' TEMPORARILY UNAVAILABLE
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Re-searched next day; see past pgs.

SESSION CONTINUES IN FILE 'WPIDS'
If this message appears repeatedly, please notify the Help Desk.
Enter "HELP STN" for information on contacting the nearest STN Help Desk by telephone or via SEND in the STNMAIL file.

=> dup rem l70,l77,l79,l80,l81
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PROCESSING COMPLETED FOR L70
PROCESSING COMPLETED FOR L77
PROCESSING COMPLETED FOR L79
PROCESSING COMPLETED FOR L80
PROCESSING COMPLETED FOR L81
L83 24 DUP REM L70 L77 L79 L80 L81 (56 DUPLICATES REMOVED)

=> d 1-24 bib abs; fil wpids

L83 ANSWER 1 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 1
AN 94:393023 BIOSIS
DN 97406023
TI Fatty acid synthesis: A potential selective target for **antineoplastic** therapy.
AU **Kuhajda F P**; Jenner K; Wood F D; Hennigar R A; Jacobs L B; Dick J D; **Pasternack G R**
CS Johns Hopkins Med. Inst., 720 Rutland Ave., Ross Building 512, Baltimore, MD 21205, USA
SO Proceedings of the National Academy of Sciences of the United States of America 91 (14). 1994. 6379-6383. ISSN: 0027-8424
LA English
AB OA-519 is a prognostic molecule found in **tumor** cells from breast **cancer** patients with markedly worsened prognosis. We purified OA-519 from human breast **carcinoma** cells, obtained its peptide sequence, and unambiguously identified it as fatty acid synthase through sequence homology and enzymology. **Tumor** fatty acid synthase is an apprxeq 270-kDa polypeptide which specifically abolished immunostaining of human breast **cancers** by anti-OA-519 **antibodies**. **Tumor** fatty acid synthase oxidized NADPH in a malonyl-CoA-dependent fashion and synthesized fatty acids composed of 80% palmitate, 10% myristate, and 10% stearate from acetyl-CoA, malonyl-CoA, and NADPH with a specific activity of 624 nmol of NADPH oxidized per min per mg. **Tumor** cell lines with elevated fatty acid synthase showed commensurate

increases in incorporation of (U-14C)acetate into acylglycerols demonstrating that fatty acid synthase increases occur in the context of overall increases in endogenous fatty acid synthesis. Cerulein inhibited acylglycerol synthesis in **tumor** cells and fibroblast controls in a dose-dependent fashion and also caused a growth inhibition which generally paralleled the level of endogenous fatty acid synthesis. Supraphysiologic levels of palmitate, 14 mu-M in dimethyl sulfoxide, significantly reversed the growth inhibition caused by cerulein at concentrations of up to 5 mu-g/ml, indicating that cerulein-mediated growth inhibition was due to fatty acid synthase inhibition.

L83 ANSWER 2 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 2
AN 92:349456 BIOSIS
DN BA94:41681
TI EXPRESSION OF ONCOGENIC ANTIGEN 519 OA-519 IN PROSTATE **CANCER** IS A POTENTIAL PROGNOSTIC INDICATOR.
AU SHURBAJI M S; **KUHAJDA F P**; **PASTERNACK G R**; THURMOND T S
CS DEP. PATHOL., J. H. QUILLEN COLL. MED., ESAT TENN. STATE UNIV., P.O. BOX 70568, JOHNSON CITY, TENN. 37614-0568.
SO AM J CLIN PATHOL 97 (5). 1992. 686-691. CODEN: AJCPAI ISSN: 0002-9173
LA English
AB Predicting the prognosis of patients with prostate **cancer** is a clinically important problem. Previous studies have indicated that the expression of haptoglobin-related protein epitopes in samples of breast **cancer** in early stages was associated with earlier relapses and higher risk for **tumor** recurrence. Oncogenic antigen 519 (OA-519) is the new marker designation for molecules expressing haptoglobin-related protein epitopes. The objective of this immunohistochemical study was to examine OA-519 expression in prostate **cancer** samples and its relationship to the established prognostic indicators of **tumor** grade, **tumor** volume, and clinical stage. Forty-two consecutive tissue samples of prostate adenocarcinoma were examined using an affinity-purified anti-OA-519 **antibody**. Twenty specimens (48%) tested positive, whereas 22 (52%) tested negative. No staining was observed in normal or hyperplastic prostate tissue. Staining occurred in 6 of 9 (67%) grade III, 14 of 23 (61%) grade II, and in none of 10 (0%) grade I cases (I vs. II and/or III: Fisher exact test, $P < 0.006$). Twenty-three of the 42 samples were transurethral resection specimens with **cancer**; 11 (48%) of these tested positive. The mean percentage of tissue chips with **tumor**, a measure of **tumor** volume, was significantly higher in the positive group (57%) than in the negative group (15%) ($P = 0.004$). The proportion of positively stained cases increased with advancing clinical stage, with 25% of Stage A cases expressing OA-519, and 46%, 67%, and 64% of Stages B, C, and D, respectively, expressing OA-519. OA-519 expression correlates with higher **tumor** grades, larger **tumors**, and possibly with advanced stage, and thus, it is potentially of prognostic value in prostate **cancer**.

L83 ANSWER 3 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 3
AN 92:282099 BIOSIS
DN BA94:6749
TI EXPRESSION OF HAPTOGLOBIN-RELATED PROTEIN IN PRIMARY AND METASTATIC BREAST **CANCERS** A LONGITUDINAL STUDY OF 48 FATAL **TUMORS**.
AU SHURBAJI M S; **PASTERNACK G R; KUHAJDA F P**
CS DEP. PATHOL., JOHNS HOPKINS HOSPITAL, 600 NORTH WOLFE ST., BALTIMORE, MARYLAND 21205.
SO AM J CLIN PATHOL 96 (2). 1991. 238-242. CODEN: AJCPAI ISSN: 0002-9173
LA English
AB The ability to establish a prognosis for patients with early breast **cancer** is an important clinical issue. Recent studies have shown that **antibodies** to haptoglobin-related protein (Hpr) may be useful in stratifying early patients with breast **cancer** according to their relative risks of recurrence. Nearly 30% of early breast **cancers** express proteins bearing Hpr epitopes. Hpr-positive breast **cancers** are more likely to recur after primary resection and are associated with shorter disease-free intervals. This immunohistochemical study examines temporal changes in Hpr expression during the course of disease in 48 patients with fatal breast **carcinoma**. Thirty-seven primary **tumors** (77%) were Hpr positive. Ten of the 11 initially negative **tumors** (91%) were Hpr positive at the time of recurrence. In contrast, only 10 of the 37 initially positive **tumors** (27%) were Hpr negative with relapse. Of 18 axillary nodes that were examined, 16 (89%) were Hpr positive; all four lymph nodal metastases in patients with initially negative primary **tumors** were Hpr positive. The authors conclude that the acquisition of Hpr expression parallels increased malignant potential and that Hpr expression, once acquired, tends to remain a permanent characteristic of any given mammary **tumor**.

L83 ANSWER 4 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 4
AN 90:444370 BIOSIS
DN BA90:95010
TI IDENTIFICATION AND PRELIMINARY CHARACTERIZATION OF TWO RELATED PROLIFERATION-ASSOCIATED NUCLEAR PHOSPHOPROTEINS.
AU MALEK S N; KATUMULUWA A I; **PASTERNACK G R**
CS DEP. PATHOL., JOHNS HOPKINS HOSPITAL, 600 N. WOLFE ST., BALTIMORE, MD. 21205.
SO J BIOL CHEM 265 (22). 1990. 13400-13409. CODEN: JBCHA3 ISSN: 0021-9258
LA English
AB Two nuclear phosphoproteins, pp35 and pp32, were purified from A20 cells, a murine B-lymphoblastoid cell line. Initially detected by cross-reactivity with **antibodies** to human erythrocyte protein 4.1, the 35- and 32-kDa proteins were purified by sequential fractionation of non-ionic detergent cell lysates on DEAE-cellulose, high performance liquid chromatography (HPLC)-anion-exchange chromatography, and HPLC hydroxylapatite chromatography. By

two-dimensional peptide mapping, pp35 and pp32 are related but do not appear to represent sequential proteolytic products. Both pp35 and pp32 appear to be associated with cell proliferation. **Antibodies** specific for pp35 and pp32 show prominent intranuclear staining in A20 cells but only focal staining in normal murine lymphoid tissues. Quantitative immunoblotting showed that both pp35 and pp32 are, respectively, expressed at 5.9 .times. 104 and 7.0 .times. 104 copies/cell in small, dense resting B lymphocytes, increasing approximately 12- and 7-fold after polyclonal stimulation with lipopolysaccharide. When normalized to total cell protein, this represents specific inductions of approximately 4- and 2-fold. Expression of both pp35 and pp32 is constitutively high in populations of **neoplastic** B cell lines; moreover, both are expressed in the nuclei of intestinal crypt epithelial cells but not in other epithelial compartments in the same sections, suggesting that forms of pp35 and pp32 may be expressed in additional tissues and associated with proliferation.

L83 ANSWER 5 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 5
AN 89:183519 BIOSIS
DN BA87:94785
TI EXPRESSION OF HAPTOGLOBIN-RELATED PROTEIN AND ITS POTENTIAL ROLE AS A **TUMOR** ANTIGEN.
AU **KUHAJDA F P**; KATUMULUWA A I; **PASTERNACK G R**
CS DEP. PATHOL., JOHNS HOPKINS UNIV. SCH. MED., 600 N. WOLFE ST., BALTIMORE, MD. 21205.
SO PROC NATL ACAD SCI U S A 86 (4). 1989. 1188-1192. CODEN: PNASA6 ISSN: 0027-8424
LA English
AB These studies describe the detection of a haptoglobin species, its characterization as the HPR gene product, and its association with both pregnancy and **neoplasia**. Previous work showed that the early recurrence of human breast **cancer** correlated with immunohistochemical staining with a commerical antiserum ostensibly directed against pregnancy-associated plasma protein A (PAPP-A). Use of this antiserum to guide purification of the putative antigen led to the present identification and purification of a strongly immunoreactive protein species distinct from PAPP-A that was present in the plasma of pregnant women at term. Unlike PAPP-A a homotetramer of 200-kDa polypeptides, the immunoreactive protein consists of a light (.alpha.) chain (16.5 kDa) and a heavy (.beta.) chain (40 kDa); protein microsequenching of the .beta. chain showed it to be a member of the hepatoglobin family. The .alpha. chain of this haptoglobin species differs from ordinary haptoglobin 1 and 2 .alpha. chains both structurally and immunologically and represents the product of the HPR gene, haptoglobin-related protein (Hpr), since (i) the apparent molecular mass is the same as that predicted for Hpr .alpha. chain, (ii) the peptide map differs from that of haptoglobin 1 in a manner predicted by the HPR nucleotide sequence, (iii) monospecific **antibodies** that react with epitopes shared by the unique .alpha. chain and a synthetic peptide derived from the HPR nucleotide sequence do not detect these epitopes in either haptoglobin 1 or 2, and (iv) sequences of .alpha.-chain peptides were consistent with

this identification, excluding haptoglobin 1 but not haptoglobin 2. The immunohistochemical reactivity of **antibodies** raised to the synthetic Hpr peptide is similar to that of anti-PAPP-A. Moreover, staining of **neoplastic** breast tissue is abolished by preincubation with purified Hpr.

L83 ANSWER 6 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 6
AN 89:126653 BIOSIS
DN BA87:61306
TI A NEW BIOMARKER IN MONITORING BREAST **CANCER** CA 549.
AU BEVERIDGE R A; CHAN D W; BRUZEK D; DAMRON D; BRAY K R; GAUR P K; ETTINGER D S; ROCK R C; SHURBAJI M S; **KUHAJDA F P**
CS C/O DAVID S. ETTINGER, MD, JOHNS HOPKINS ONCOL. CENT., 600 N. WOLFE ST., ROOM 130, BALTIMORE, MD. 21205, USA.
SO J CLIN ONCOL 6 (12). 1988. 1815-1821. CODEN: JCONDN ISSN: 0732-183X
LA English
AB Serum biomarkers are not very reliable in assessing outcome or predicting recurrence of breast **cancer**. Clinically, **carcinoembryonic** antigen (CEA) is widely used and is elevated in a majority of patients with metastatic breast **cancer**. However, it is falsely elevated in a wide range of nonmalignant conditions and correlates poorly with disease progression. We evaluated a newly described monoclonal **antibody**, CA 549, in an immunoradiometric assay which uses two monoclonal **antibodies** directed against **tumor** and milk fat globule membranes. CA 549 and CEA were studied in 682 patients, 331 of whom had breast diseases and 99 of whom were followed with multiple serum samles. Of 69 patients with benign breast diseases, 1.5% had elevated CA 549, 0% of 30 pregnant women had elevated CA 549, and 26% of patients with nonmalignant liver disease had CA 549 elevation. In metastatic **cancer** of prostate, ovary, endometrium, colon, and lung CA 549 was elevated in 12% to 50% of cases with levels < 120 U/mL. In breast **cancer**, CA 549 was elevated in 11% of 88 patients who received adjuvant chemotherapy and had no evidence of metastasis; in 23% of 16 patients in complete remission after chemotherapy; in 63% of 52 patients in partial remission after therapy; and in 83% of 106 patients with progression of breast **cancer** compared with 63% with elevated CEA (P = .001). In diseases of the breast, CA 549 has a sensitivity and specificity of 77% and 92% v 61% and 92% for CEA. Of 99 patients serially monitored with clinically documented breast **cancer** progression, regression, or stability of disease, CA 549 was statistically significantly superior to CEA in monitoring a > 25% change in those patients with metastatic progression (P = .03). CA 549 is a new serum marker that should be control tested in prospective clinical trials alone or in conjunction with other markers.

L83 ANSWER 7 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS
AN 88:195020 BIOSIS
DN BR34:98207
TI DETECTION OF CA-549 IN EPITHELIAL **NEOPLASM** BY EIA SERUM ASSAY AND IMMUNOHISTOCHEMISTRY.

AU SHURBAJI M S; BEVERIDGE R A; CHAN D W; **KUHAJDA F P**
CS JOHNS HOPKINS HOSP., BALTIMORE, MD.
SO 77TH ANNUAL MEETING OF THE USA AND CANADIAN ACADEMY OF PATHOLOGY (USA-CANADIAN DIVISION OF THE INTERNATIONAL ACADEMY OF PATHOLOGY), WASHINGTON, D.C., USA, FEBRUARY 28-MARCH 4, 1988. LAB INVEST 58 (1). 1988. 85A. CODEN: LAINAW ISSN: 0023-6837
DT Conference
LA English

L83 ANSWER 8 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS
AN 88:194817 BIOSIS
DN BR34:98004
TI CA-549 IN BREAST **CARCINOMA** SERUM LEVELS AND IMMUNOHISTOCHEMISTRY.
AU **KUHAJDA F P**; SHURBAJI M S; BEVERIDGE R A; CHAN D W
CS JOHNS HOPKINS HOSP., BALTIMORE, MD.
SO 77TH ANNUAL MEETING OF THE USA AND CANADIAN ACADEMY OF PATHOLOGY (USA-CANADIAN DIVISION OF THE INTERNATIONAL ACADEMY OF PATHOLOGY), WASHINGTON, D.C., USA, FEBRUARY 28-MARCH 4, 1988. LAB INVEST 58 (1). 1988. 51A. CODEN: LAINAW ISSN: 0023-6837
DT Conference
LA English

L83 ANSWER 9 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 7
AN 87:253209 BIOSIS
DN BA84:6181
TI COMMON LEUKOCYTE ANTIGEN STAINING OF A PRIMITIVE SARCOMA.
AU MCDONNELL J M; BESCHORNER W E; **KUHAJDA F P**; DEMENT S H
CS DEP. PATHOL., JOHNS HOPKINS MED. INST., BALTIMORE, MD. 21205.
SO CANCER (PHILA) 59 (8). 1987. 1438-1441. CODEN: CANCAR ISSN: 0008-543X
LA English
AB A 4-year-old boy presented with symptoms of tracheal obstruction and was found to have a polypoid tracheal mass, which was studied by biopsy. Light microscopy showed a **tumor** composed of small cells with round to oval dark nuclei, clumped chromatin, one to two nucleoli, and small, variable amounts of indistinct pink cytoplasm. In other areas the **tumor** had a loose, spindle appearance, with some cells showing more elongated nuclei, and fibrillar pink cytoplasm consistent with strap cells. Cross striations were not found. Electron microscopy showed desmosomes and 7 to 10 nm cytoplasmic filaments forming dense bodies. The findings are most consistent with a primitive sarcoma, probably rhabdomyosarcoma. Immunoperoxidase with three monoclonal **antibodies** for common leukocyte antigen showed diffuse membraneous staining with fresh-frozen tissue. All other lymphocyte and monocyte marker studies were negative. We believe that this case of anticommon leukocyte antigen staining, a rhabdomyosarcoma, represents the first report of a false positive reaction with monoclonal **antibody** to common leukocyte antigen.

L83 ANSWER 10 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 8
AN 87:486105 BIOSIS

DN BA84:120748
TI PRIMARY LYMPHOMAS OF THE LIVER REPORT OF SIX CASES AND REVIEW OF THE LITERATURE.
AU DEMENT S H; MANN R B; STAAL S P; **KUHAJDA F P**; BOITNOTT J K
CS DEP. PATHOL., JOHNS HOPKINS HOSP., BALTIMORE, MD. 21205.
SO AM J CLIN PATHOL 88 (3). 1987. 255-263. CODEN: AJCPAI ISSN: 0002-9173
LA English
AB Six cases of diffuse large cell lymphoma (DLCL) of the liver were studied with immunohistochemistry for common leukocyte antigen (CLA), lysozyme, alpha-1-antitrypsin (AAT), and kappa and lambda light chains on paraffin-embedded tissues. All six cases were positive for CLA. Four of the six cases showed staining for lysozyme and ATT (three focal and one diffuse staining). In three cases, frozen tissue for monoclonal **antibodies** and glutaraldehyde-fixed tissue for electron microscopic examination were available. Two of these showed B-cell phenotypes with monoclonal **antibody** studies. Electron microscopic examination on these two B-cell lymphomas showed scant cytoplasm and a paucity of cytoplasmic organelles. The third case did not show definite B- or T-cell surface markers but did show strong Leu-M1 and OKM1 staining. Electron microscopic examination of the **tumor** cells showed a prominent Golgi apparatus, abundant cytoplasm with numerous cytoplasmic organelles and phagolysosomes. However, DNA hybridization studies of this **tumor** showed immunoglobulin heavy and kappa light chain gene rearrangements typical of a B-cell lymphoma. All six lymphomas were solitary liver masses without evidence of disease elsewhere. The mean age for the six patients was 56.2 years (four males, two females).

L83 ANSWER 11 OF 24 MEDLINE DUPLICATE 9
AN 87207523 MEDLINE
TI Immunocytochemistry of normal pancreatic islets and spontaneous islet cell **tumors** in dogs.
AU Hawkins K L; Summers B A; **Kuhajda F P**; Smith C A
SO Vet Pathol, (1987 Mar) 24 (2) 170-9.
Journal code: XBQ. ISSN: 0300-9858.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8708
AB Immunocytochemical studies of the distribution of glucagon, gastrin, insulin, and somatostatin in normal canine pancreatic islets and 20 canine islet cell **tumors** were done using the peroxidase-anti-peroxidase (PAP) technique. In the normal adult canine pancreas, islets typically consisted of clusters of 20-30 cells, but smaller foci and even individual cells were identified. Alpha cells (glucagon) were often peripherally located, beta cells (insulin) were centrally located and most numerous, and delta cells (somatostatin) were the least numerous and randomly located. Both juvenile and adult canine pancreases did not stain for gastrin. Of the 20 **tumors** examined, 18 had positive immunoreactivity for insulin, nine for glucagon, 14 for somatostatin, and one for

gastrin. Two **tumors** were uninterpretable due to autolysis. Three **tumors** were pure insulinomas, but no pure somatostatinomas, glucagonomas, or gastrinomas were identified. Most **tumors** and metastases had mixed positive immunoreactivity; one **neoplastic** cell type predominated with lesser numbers of other cell types. Metastatic sites (liver and lymph node) stained for insulin and somatostatin, only. Foci of non-**neoplastic** islet cell tissue (nesidioblastosis), often located at the pancreatic-mesenteric junction, stained strongly positive for insulin, glucagon, and somatostatin but not for gastrin. The **tumor** staining pattern did not consistently correlate with **tumor** function, as determined by blood glucose and serum insulin assays. The PAP technique works well on paraffin-embedded, formalin-fixed tissue using rabbit or guinea pig antisera as the primary **antibody**. Staining occurred on sections of paraffin blocks stored for up to 7 years.

L83 ANSWER 12 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 10
AN 85:344641 BIOSIS
DN BA80:14633
TI LOCALIZATION OF A MEMBRANE GLYCOPROTEIN IN BENIGN FIBROCYSTIC DISEASE AND INFILTRATING DUCT **CARCINOMAS** OF THE HUMAN BREAST WITH THE USE OF A MONOCLONAL **ANTIBODY** TO GUINEA-PIG MILK FAT GLOBULE MEMBRANE.
AU GREENWALT D E; JOHNSON V G; **KUHAJDA F P**; EGGLESTON J C; MATHER I H
CS DEP. ANIM. SCI., UNIV. MD., COLLEGE PARK, MD. 20742.
SO AM J PATHOL 118 (3). 1985. 351-359. CODEN: AJPAA4 ISSN: 0002-9440
LA English
AB With monoclonal **antibody** D-274, raised against guinea pig milk fat globule membrane, the distribution of mucinlike glycoproteins of MW .gtoreq. 400,000 was determined in benign fibrocystic disease and infiltrating duct **carcinoma** of the human breast. These glycoproteins, called collectively PAS-I, were detected in 19 of 20 cases of benign fibrocystic disease and in at least 26 of 47 cases of infiltrating duct **carcinoma**. PAS-I was concentrated on luminal surfaces of ducts and alveoli in morphologically differentiated regions of the **tumors**. In areas where the glandular nature of the tissue was less evident in infiltrating duct **carcinoma**, the PAS-I determinant recognized by **antibody** D-274 was present on irregular luminal surfaces and in the cytoplasm. There was a negative correlation between the short-term recurrence (< 2 yr) of infiltrating duct **carcinoma** and the detection of strong positive staining with **antibody** D-274. The results are discussed with reference to recent studies on PAS-I in human breast tissue using monoclonal **antibodies** raised against human milk fat globule membrane.

L83 ANSWER 13 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 11
AN 84:187806 BIOSIS
DN BA77:20790
TI THE DISTRIBUTION OF **CARCINO** EMBRYONIC ANTIGEN IN BREAST

CARCINOMA DIAGNOSTIC AND PROGNOSTIC IMPLICATIONS.
AU **KUHAJDA F P**; OFFUTT L E; MENDELSOHN G
CS PATHOL. DEP., JOHNS HOPKINS HOSP., 600 N. WOLFE ST., BALTIMORE, MD. 21205.
SO CANCER (PHILA) 52 (7). 1983. 1257-1264. CODEN: CANCAR ISSN: 0008-543X
LA English
AB **Carcinoembryonic** antigen (CEA) has been shown to be a useful **tumor** marker in patients with breast **carcinoma**. The unlabeled **antibody** immunoperoxidase technique was used to localize CEA in 93 cases of primary breast **carcinoma**, 15 cases of atypical duct papillomatosis and 4 cases of duct papilloma. Normal breast epithelium and breast epithelium in fibrocystic disease did not stain positively for CEA. Twenty-four of 27 (88%) intraductal **carcinomas**, and 47 of 69 (68%) infiltrating duct **carcinomas** were CEA positive. In contrast, only 5 of 21 (23%) in situ lobular **carcinomas** and 8 of 24 (33%) infiltrating lobular **carcinomas** were positive for CEA. All 15 cases of atypical epithelial papillomatosis were negative, whereas 1 of the 4 cases of duct papilloma exhibited microscopic foci of weak CEA positivity. There was a trend for infiltrating duct **carcinomas**, .ltoreq. 3 cm in diameter, staining strongly positive for CEA, to be associated with synchronous axillary lymph node metastases (P = 0.09). **Tumor** heterogeneity was a constant feature of CEA staining with positivity varying from region to region and even from cell to cell. Positive immunohistochemical staining for CEA may play an adjunctive role in discriminating intraductal **carcinoma** from atypical papillary ductal proliferations.

L83 ANSWER 14 OF 24 CANCERLIT
AN 78626615 CANCERLIT
TI ON THE SUPPRESSION OF **TUMOR** CELLS IN VITRO BY MACROPHAGES AND ANTISERUM.
AU **Pasternack G R**
CS John Hopkins Univ., Baltimore, MD
SO Diss Abstr Int (Sci), (1978). Vol. 39, No. 2, pp. 653B-654B.
DT (THESIS)
FS ICDB
LA English
EM 7811
AB The suppression of **tumor** cells by antiserum and macrophages was studied in vitro. Line 1 lymphosarcoma cells, derived from the murine lymphosarcoma 6C3HED, were incubated with peritoneal exudate macrophages induced by starch in C57Bl/6 mice and C57Bl/6-anti-6C3HED. **Tumor** cells so incubated were shown to undergo a profound suppression characterized by the failure to incorporate radiolabeled iododeoxyuridine. Suppression became evident within several hours after incubation had begun. Studies using anti-Thy-1 antiserum and complement demonstrated that T cells were not involved in this process. Dose response curves showed that suppression was one-hit with respect to macrophages, and multi-hit with respect to antiserum. Phagocytosis and primary lysis were

excluded as mechanisms of suppression. Cell contact was required for the initiation of **tumor** suppression. This step was followed by a second step in which the suppressed state became fully manifest; this second step appeared to be independent of cell contact. Supernatants from a variety of macrophage preparations were unable to duplicate this suppression. Suppressed cells were purified by glass bead columns and shown to exclude dye but to have impaired growth properties. Cloning experiments showed that this was due to a stable population of cells that excluded dye but did not proliferate, regardless of the degree of suppression in the initial reaction. Suppressed cells were shown to incorporate labeled uridine and leucine but not thymidine. Also, suppressed cells were shown to oxidize glucose. Attempts to induce suppressed cells to proliferate by stimulation with mitogens were unsuccessful. Suppressed cells died in prolonged culture through secondary lysis, which was designated the third step in this mechanism. These studies describe a mechanism of **tumor** suppression by **antibody** and macrophages and resolve that mechanism into three distinct steps. **Tumor** cells in the suppressed state, an intermediate stage between the initiation of the process and cell death, were isolated and characterized in terms of their metabolic functions. This mechanism may be of potentially great significance in **antibody**-mediated lymphoma suppression in vivo. (Author abstract) (no Refs)

L83 ANSWER 15 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 12
AN 78:228379 BIOSIS
DN BA66:40876
TI **TUMOR** CELL CYTO STASIS BY MACROPHAGES AND **ANTIBODY** IN-VITRO PART 2 ISOLATION AND CHARACTERIZATION OF SUPPRESSED CELLS.
AU **PASTERNACK G R**; JOHNSON R J; SHIN H S
CS DEP. MICROBIOL., JOHNS HOPKINS UNIV. SCH. MED., BALTIMORE, MD. 21205, USA.
SO J IMMUNOL 120 (5). 1978 1567-1572. CODEN: JOIMA3 ISSN: 0022-1767
LA English
AB **Tumor** cells [line 1 mouse lymphoblastoid cells] in a cytostatic state caused by [mouse] macrophages and **antibody** were isolated. Such suppressed cells excluded vital dye, incorporated uridine and leucine and metabolized glucose. They did not, however, incorporate thymidine or resume cell division in culture. During prolonged culture, these cells eventually died. In this system, cytostasis was an all-or-nothing phenomenon at the level of the individual cell. Once in the cytostatic state **tumor** cells did not resume proliferation.

L83 ANSWER 16 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 13
AN 78:228378 BIOSIS
DN BA66:40875
TI **TUMOR** CELL CYTOSTASIS BY MACROPHAGES AND **ANTIBODY** IN-VITRO PART 1 RESOLUTION INTO CONTACT DEPENDENT AND CONTACT INDEPENDENT STEPS.
AU **PASTERNACK G R**; JOHNSON R J; SHIN H S
CS DEP. MICROBIOL., JOHNS HOPKINS UNIV. SCH. MED., BALTIMORE, MD. 21206,

USA.
SO J IMMUNOL 120 (5). 1978 1560-1566. CODEN: JOIMA3 ISSN: 0022-1767
LA English
AB In a murine system, macrophages, in concert with **antibody**, suppressed iododeoxyuridine incorporation by **tumor** cells [line 1 mouse lymphoblastoid cells]. The mechanism of suppression did not involve phagocytosis or lysis. The generation of suppressed **tumor** cells was resolved into a contact-dependent step and a contact-independent step. The 1st step was 1-hit with respect to macrophages and multi-hit with respect to **antibody**.

L83 ANSWER 17 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 14
AN 79:58078 BIOSIS
DN BR16:58078
TI MECHANISMS OF **TUMOR** IMMUNITY THE ROLE OF **ANTIBODY** AND NONIMMUNE EFFECTORS.
AU SHIN H S; JOHNSON R J; **PASTERNACK G R**; ECONOMOU J S
SO KALLOS, PAUL, BYRON H. WAKSMAN AND ALAIN L. DE WECK (ED.). PROGRESS IN ALLERGY, VOL. 25. XIV+242P. ILLUS. S. KARGER: BASEL, SWITZERLAND; NEW YORK, N.Y., USA. 1978 163-210 ISBN: 3-8055-2849-3
LA Unavailable

L83 ANSWER 18 OF 24 MEDLINE DUPLICATE 15
AN 79055104 MEDLINE
TI Mechanisms of **tumor** immunity: the role of **antibody** and nonimmune effectors.
AU Shin H S; Johnson R J; **Pasternack G R**; Economou J S
SO Prog Allergy, (1978) 25 163-210. Ref: 286
Journal code: PZS. ISSN: 0079-6034.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
EM 7903

L83 ANSWER 19 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 16
AN 77:175359 BIOSIS
DN BA63:70223
TI **ANTIBODY** MEDIATED SUPPRESSION OF **TUMOR** GROWTH PART 3 MOLECULAR ASSAY OF MURINE IMMUNO GLOBULIN G-1 ALLO **ANTIBODY** REQUIRED TO CAUSE **TUMOR** SUPPRESSION IN-VIVO.
AU JOHNSON R J; **PASTERNACK G R**; DRYSDALE B-E; SHIN H S
SO J IMMUNOL 118 (2). 1977 498-504. CODEN: JOIMA3 ISSN: 0022-1767
LA Unavailable
AB A radioimmunoassay was used to quantitate the number of [mouse lymphoma 6C3HED] **tumor** cell-bound IgG1 [immunoglobulin G1] anti-**tumor** **antibody** molecules required to cause suppression of **tumor** growth in C3H mice. Radiolabeled anti-IgG1 was used to detect cell-bound IgG1 **antibody**. The assay was calibrated by using TNP[trinitrophenol]-coupled **tumor** cells that had a known number of bound IgG1 anti-DNP [dinitrophenol] molecules. From 70,000-130,000 IgG1 anti-

tumor antibody molecules per **tumor** cell were sufficient to cause 50% suppression of **tumor** growth in mice inoculated with approximately 50,000 **tumor** cells.

L83 ANSWER 20 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 17
AN 77:175358 BIOSIS
DN BA63:70222
TI **ANTIBODY** MEDIATED SUPPRESSION OF **TUMOR** GROWTH PART 2 MACROPHAGE AND PLATELET COOPERATION WITH MURINE IMMUNO GLOBULIN G-1 ISOLATED FROM ALLO ANTI SERUM.
AU JOHNSON R J; **PASTERNACK G R**; SHIN H S
SO J IMMUNOL 118 (2). 1977 494-497. CODEN: JOIMA3 ISSN: 0022-1767
LA Unavailable
AB The effectors that cooperate with IgG1 [immunoglobulin G1] in causing **tumor** [mouse 6C3HED lymphoma] suppression were identified as exudate macrophages and blood platelets in mice syngeneic and allogeneic to the **tumor**. Lymphocytes were not active in suppressing **tumor** growth in the presence of IgG1 **antibody**, although they were active with whole antiserum.

L83 ANSWER 21 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 18
AN 77:175357 BIOSIS
DN BA63:70221
TI **ANTIBODY** MEDIATED SUPPRESSION OF **TUMOR** GROWTH PART 1 SUPPRESSION BY MURINE IMMUNO GLOBULIN G-1 ISOLATED FROM ALLO ANTI SERUM.
AU JOHNSON R J; **PASTERNACK G R**; SHIN H S
SO J IMMUNOL 118 (2). 1977 489-493. CODEN: JOIMA3 ISSN: 0022-1767
LA Unavailable
AB The **tumor** suppressive activity of murine IgG1 [immunoglobulin G1] **antibody** was studied in vivo. IgG1 was isolated from hyperimmune alloantisera against murine lymphoma 6C3HED cells by absorption with heat-killed, formalinized Staphylococcus aureus Cowan strain I, followed by DEAE ion exchange chromatography and Sephadex G-200 gel filtration chromatography. The isolated IgG1, which had no detectable IgM, IgA, IgG2a, IgG2b or IgG3, could suppress the growth of the **tumor**. DEAE and Sephadex G-200 column profiles of the in vivo **tumor** suppressive activity showed good correlation with the profiles of total IgG1 and anti-**tumor antibody** assayed for IgG1 H chains and .kappa. L chains. The IgG1 **tumor** suppressive activity was not diminished after heating at 56.degree. C for 30 min.

L83 ANSWER 22 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 19
AN 77:132877 BIOSIS
DN BA63:27741
TI **ANTIBODY** MEDIATED SUPPRESSION OF GRAFTED LYMPHOMA PART 4 INFLUENCE OF TIME OF **TUMOR** RESIDENCY IN-VIVO AND **TUMOR** SIZE UPON THE EFFECTIVENESS OF SUPPRESSION BY SYNGENEIC **ANTIBODY**.
AU SHIN H S; ECONOMOU J S; **PASTERNACK G R**; JOHNSON R J; HAYDEN M L
SO J EXP MED 144 (5). 1976 1274-1283. CODEN: JEMEAV ISSN: 0022-1007

LA Unavailable
AB In the suppression of the growth of a mouse lymphoma 6C3HED by **antibody**, the effectiveness of **antibody** in suppressing growing or established **tumor** cells and a comparable number of freshly injected **tumor** cells is quantitatively similar. The effectiveness of **antibody** diminishes markedly when the number of **tumor** cells per mouse reaches the level of 106 due to the development of a macrophage shortage. At the 105 **tumor** cell level (**antibody** -mediated suppression takes place in an optimal manner and between 105 and 104 **tumor** cell numbers) the amount of **antibody** required to suppress 50% of the **tumor** cells is directly proportional to the number of **tumor** cells suppressed.

L83 ANSWER 23 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS
AN 76:36765 BIOSIS
DN BR12:36765
TI **TUMOR** CELL CYTO TOXICITY BY MACROPHAGES AND **ANTIBODY** A NONLYTIC NONPHAGOCYTIC MECHANISM.
AU **PASTERNACK G R**; BUKOWSKI J; SHIN H S
SO FED PROC 35 (3). 1976 471 CODEN: FEPRA7 ISSN: 0014-9446
DT Conference
LA Unavailable

L83 ANSWER 24 OF 24 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 20
AN 77:127170 BIOSIS
DN BA63:22034
TI IMMUNO THERAPY OF **CANCER** WITH **ANTIBODY**.
AU SHIN H S; **PASTERNACK G R**; ECONOMOU J S; JOHNSON R J; HAYDEN M L
SO SCIENCE (WASH D C) 194 (4262). 1976 327-329. CODEN: SCIEAS ISSN: 0036-8075
LA Unavailable
AB A long-term suppression of a transplanted solid **tumor** that was growing in a syngeneic mouse can be achieved by the administration of **antibody** against the **tumor**. The susceptibility of such growing **tumor** cells to **antibody** treatment is similar to that of a comparable number of freshly injected **tumor** cells.

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